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THE HYPERVENTILATION SYNDROME.

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THAT certain unpleasant symptoms resulted from hyperventilation and the ensuing hypocapnia was well known to physiologists of the last century. However, the syndrome as a clinical entity or symptom complex was first described by Kerr and his associates in 1937 (Kerr *et alii*, 1937).

This syndrome occurs as paroxysmal bouts of hyperventilation which is generally due to an emotional stimulus, with a symptom complex largely caused by the alkalosis consequent upon the hypocapnia.

A great amount of literature has been written on this subject since then; but it is by no means disproportionate considering the frequency of occurrence of this syndrome.

The present series of 50 cases was collected in about two and a half years in a solo general practice. In that same time about a dozen cases of acute appendicitis were encountered. The importance of the syndrome lies, not only in its frequency of occurrence, but also in the fact that much can be done to help the sufferers.

Diagnosis.

Any "turns" during which the patient complains of some of the following symptoms should be suspected as being cases of the hyperventilation syndrome: tremors; exhaustion; light-headedness; apprehension; shortness of breath; excessive sighing with or without yawning; palpitations; sweating; hot feelings; cold feelings; dryness of the mouth; blurred vision; paræsthesias; giddiness; nausea with or without vomiting; skeletal pain; tinnitus; frequency of micturition with or without diuresis; headache; aerophagy (bloating, belching or flatulence); syncope; globus hystericus; tetany; alimentary colic.

If, from the history, this syndrome is suspected, diagnostic confirmation is made by the reproduction of an acute exacerbation of the patient's symptoms; this is done by getting him voluntarily to overbreathe for a few minutes. It is necessary in this procedure for the pulmonary ventilation to be at least doubled, and many patients soon become aware that the procedure is going to be uncomfortable, and resist.

They resist by apparently indulging in forced respiratory effort, but in fact they use only their accessory respiratory muscles. In this way they do not increase their pulmonary ventilation appreciably. It was found helpful in these cases to obtain the patient's confidence by palpating his radial pulse throughout the procedure so that he "would not come to any harm". It was found helpful also actually to hyperventilate with him to show what was required of him. In a few resistant cases firm encouragement was found necessary.

Only if the syndrome is not reduplicated at the end of three minutes of adequate breathing was the result of the test considered negative.

If a characteristic attack is induced, the patient is given a large plastic bag to breathe from and into. A satisfactory bag is one measuring 2 feet by 1 foot and having a volume when full of approximately 10 litres; tied into the open end is a length of about six inches of wide-bore (half to three-quarters of an inch) tubing or hose. It is important in this procedure for the patient to hold his nose and to make sure that no air escapes between the tubing and his lips. This can be achieved by his blowing into and sucking from the bag rather than breathing into it. This can be done either quietly or strenuously as the patient desires. By this rebreathing process the alveolar carbon dioxide level returns to normal and the patient is told to stop when the symptoms abate.

In some cases the syndrome is not exactly reduplicated by such means. However, in the taking of the history it was found that the episodes in the same patient varied slightly; and also the induced attack takes place in the reassuring presence of a physician. This alteration in environment is sufficient to account for the slight differences between a natural attack and an induced attack.

The heralding symptoms in this series were as follows: apprehension in 15 cases; a hot feeling in 14 cases; light-headedness in 10 cases; giddiness in two cases; headache in two cases; musculo-skeletal symptoms in two cases; tinnitus in one case; blurred vision in one case; a cold feeling in one case.

TABLE I.

Percentage Incidence of Symptoms in Present Series.

Symptom.	Number of Cases.	Percentage Incidence.
Central nervous system:		
Light-headedness	45	90
Syncope	13	26
Giddiness	24	48
Sweating	34	68
Tinnitus	18	36
Headache	16	32
Blurred vision	26	52
Apprehension	44	88
Exhaustion	46	92
Peripheral neuro-vascular system:		
Paræsthesia	24	48
Hot feeling	33	66
Cold feeling	29	58
Musculo-skeletal system:		
Tetany	9	18
Tremors	47	94
Skeletal pain	18	36
Cardio-vascular system:		
Palpitations	38	76
Respiratory system:		
Shortness of breath	43	86
Excessive sighing and/or yawning	41	82
Alimentary system:		
Dryness of mouth	28	56
Globus hystericus	9	18
Aerophagy	15	30
Colic	6	12
Nausea and/or vomiting	19	38
Urinary system:		
Frequency of micturition and/or diuresis	16	32

Description of Series.

In six cases the patients were either examined during or interviewed about their first attack, whilst in others the patients had had several bouts per week over a period of many years. Those patients who had had only a few attacks (up to six) were able to specify the exact number, and were also able to relate exactly when they had occurred. As one would expect, as the number of attacks complained of increased, the accuracy of the patient's estimate decreased.

The group contained a preponderance of females in a ratio of approximately 7:1 (44 females and six males).

The average age of the patients in this series was 37 years; the two extremes of age were 17 and 89 years. Whilst the upper extreme of age is the greatest age of a sufferer observed by the author, the lower limit in the series does not represent the earliest age. A girl aged six years with this complaint was encountered a few years ago, but she is not included in this series.

The time interval between the occurrence of the first attack and the present was noted. This varied from zero to 50 years, with an average of two years. The average duration of an acute episode was about 30 minutes; the limits were three and 120 minutes. Many factors prevented this estimate from being accurate. In all but a few cases the patient himself estimated the time, and since anxiety is a common feature of the syndrome, then this estimate was open to doubt. Another factor operating against the accurate estimate of duration was the fact that in some cases the patient complained of the symptoms "on and off" for some considerable time—for example, "all day" or "all night". The times of the onset and the termination of the attacks were difficult to appraise. In any case, what criterion is one to take as the indication of the termination of the acute episode? The exhaustion may last for days, the diuresis may last for half a day, and most of the other symptoms are gradual in their disappearance.

Discussion of Symptoms.

Light-Headedness.

Hypocapnia causes constriction of cerebral blood vessels and a considerable reduction in blood flow through the brain. Light-headedness may to some extent be due to the effect of this reduced blood flow on the central nervous system short of actual syncope.

Under this heading have been included other symptoms arising from the same cause—faintness, impairment of concentration or memory and a feeling of unreality. In one particular case a patient said that during an attack she knew what to say, but could not say it. Many patients volunteered dizziness as one of their symptoms. On closer questioning, some of these admitted that their dizziness in fact was light-headedness and not a true vertigo.

Syncope.

As is the case with light-headedness, syncope is probably due in part to the effect of reduced blood flow on the central nervous system. This symptom occurred in 13 of the cases. In these 13 cases syncope did not occur with every attack, but it has been included in the summary if it occurred in any previous hyperventilation episode. Some patients suffering from this syndrome are unable voluntarily to cease hyperventilating. In these cases syncope serves as a protective mechanism. During the period of unconsciousness apnœa occurs and the partial pressure of carbon dioxide in the blood arises. As one would expect, this symptom never occurred as a heralding symptom.

Giddiness.

Vertigo occurred in 24 cases. In a few cases this was present only when the patient was sitting or standing and disappeared when he assumed the prone position.

Sweating.

The sites of the sweating, in descending order of frequency, were as follows: the hands, the head, the whole body, the feet. The hands and axillæ are recognized as being the classical sites of sweating which is due to anxiety rather than temperature regulation. It was noted that the sweating was symmetrical in its distribution, and also that it had no consistent relationship with the symptom of feeling cold. Sometimes this symptom was expressed as a feeling of clamminess; and it never occurred as a heralding symptom in any case in this series.

Headache.

Headache occurred in 16 cases. Two of the patients who complained of headache were found, on closer questioning, to be suffering from paræsthesia of the scalp.

Apprehension.

Apprehension occurred in 44 of the cases. It was most commonly expressed as a fear, and during an induced attack it was manifested as a restlessness. During the induced attack many of the patients crossed and recrossed their legs and shifted about on the chair or couch in an agitated manner.

This is the symptom which showed the most variation between an induced attack and a natural attack. It is the symptom which one would expect to be influenced most by the psychological environment of the patient. It occurred less frequently in the induced attack, which took place in the presence of the physician, than it did in the natural attack, which in some cases took place when the patient was alone at home at night. Some patients said that they thought that they were going to die in an attack; others said that they thought their hearts were going to stop.

Exhaustion.

Exhaustion occurred in 46 cases and, next to tremors, it was the most common symptom. There was a considerable variation in the extent of this symptom. In some cases it was merely a slight tiredness of short duration, while in others it was a complete exhaustion which was sufficient to send the patient to bed for days afterwards. Depression often accompanied this exhaustion. This symptom always occurred late in the episode, and, together with diuresis, was the only symptom present when all the others had disappeared. The disturbance in blood chemistry would not last for days, and the muscular effort involved in the hyperventilation could not account for the degree and duration of the exhaustion met in some cases.

Paræsthesia.

Paræsthesia occurred in 24 cases, and was variously described as numbness, pins and needles, tingling, itching and "something crawling on me". In two cases the paræsthesia was asymmetrical—a fact which indicates that its origin is probably peripheral and not central. It is interesting to note that it was commonest in the areas in which sensory perception is greatest. The paræsthesia was present in different sites in the same patient and the order of frequency of the sites was as follows: the upper extremity in 21 cases; the lower extremity in 10 cases; the perioral area in seven cases; the scalp in four cases; the face other than the perioral area in two cases; the tongue in two cases; the trunk in one case. These sites followed the pattern that has been described by others. Only rarely did the paræsthesia in the upper extremity extend above the elbow, and only rarely did the paræsthesia in the lower extremity extend above the knee.

Hot and Cold Feelings.

The commonest finding was that of a hot feeling followed by a cold feeling (involving the whole body in 12 cases and localized in two cases).

The next most frequent phenomenon was that of a hot feeling only (involving the whole body in seven cases and localized in six cases), and even if this was localized it always occurred in the face.

In nine cases the cold feeling only occurred, and this was generalized in every case. The hot and cold feeling occurred simultaneously in different parts of the body in one case; and in two cases the hot and cold feelings occurred alternately. The cold feeling preceded the hot feeling in two cases.

It is interesting to note that whenever localization of these feelings occurred, the site in every case was above the waist.

These phenomena could not all be explained as vasomotor reactions, especially when the hot and cold feelings occurred simultaneously in the one patient.

Tetany.

In nine cases only did frank tetany occur—a finding which rather explodes the prevalent misconception that hyperventilation syndromes are characterized by acute, dramatic but transitory bouts of hyperpnœa culminating in frank tetany. Of these nine patients, eight showed localized tetany, and in one case only was the tetany generalized. In this one case generalized muscular rigidity occurred, involving the trunk (giving rise to opisthotonos) and the extremities.

In Cases IX, XXVI, XXIX and XXXVIII the tetany occurred only in the hands (carpo-pedal spasm). In Case XVI tetany occurred in the muscles of the chest and the upper extremity. In Case XIX it occurred in the hand, the lower extremity and the chest; in Case XXV it occurred in the lower extremity only; and in Case XXXIII in the muscles of the upper extremity. It will be seen from this that out of the nine cases carpo-pedal spasm occurred in eight. In other cases latent tetany was shown to be present by one or other of the following tests: (i) Trousseau's sign (the appearance of carpo-pedal spasm—the *main d'accoucheur*) when the blood supply to the hand is impeded by pressure on the brachial artery, or by the rapid elevation of the pressure in a sphygmomanometer cuff); (ii) Chvostek's sign (the contraction of the facial muscles in response to tapping over the facial nerve as it emerges from the stylomastoid foramen). In the literature puckering of the lips has been mentioned as a moderately common form of localized tetany; but no case of this nature was met with in the present series.

Tremors.

Tremor was the most common of all the symptoms, occurring in 47 cases. The sites of the tremors were as follows. They were generalized in 34 cases; they occurred in both extremities in three cases, in the upper extremity in one case and in the lower extremity in two cases. They occurred in the hands only in three cases, in the hand and the jaw in one case, in the hands and the abdominal muscles in one case, in the hands and the head in one case and in the extremities and the abdominal muscles in one case.

Skeletal Pain.

Skeletal pain occurred in 18 cases, as follows: in the chest muscles (bilateral) anteriorly in four cases; in the abdominal muscles in two cases; in the dorsal region of the back in one case; in the chest muscles (left side) in 10 cases; in the chest (right side) anteriorly and posteriorly in one case.

Palpitations.

Palpitations occurred in 38 cases, and in nearly every case this symptom was volunteered rather than admitted in response to a leading question.

Shortness of Breath.

This symptom, occurring in the absence of exertion, was admitted or volunteered in 43 cases. The hyperventilation was sometimes described as a suffocating or smothering feeling or an inability to take a deep breath. Some patients said that during an attack they had a strong desire to get outside or to open the window. In seven cases the patient did not complain of or admit to shortness of breath, even in spite of the fact that increased pulmonary ventilation must have occurred. However, in four of these cases the patient did admit to sighing during the attack itself. Undoubtedly this increased the pulmonary ventilation in these cases. There still remained three cases in which the altered pulmonary ventilation did not reach consciousness.

Thus, in the series of 50 cases under discussion the altered pulmonary ventilation in three cases did not reach consciousness; and in a further four cases it was described as a sighing. In many others the altered pulmonary ventilation was admitted only in response to a leading question. This is consistent with Evans's (1947) statement: "We are not generally aware of an increase in the volume of the pulmonary ventilation until this has been about doubled." In none of these cases did the patient claim an aberration of breathing to be the heralding symptom.

Excessive Sighing and/or Yawning.

Although excessive sighing or yawning occurred only occasionally during the acute bout, it was a very common feature in these patients at other times. It is mentioned here because these symptoms are obviously manifestations of a respiratory neurosis or a respiratory instability. These activities are present in normal people, but usually occur in response to a particular psychological stimulus. Their presence in these patients occurred when this psychological stimulus was lacking.

Dryness of the Mouth.

Dryness of the mouth may have been due in some cases to mouth breathing during the hyperventilation.

Globus Hystericus.

This was described either as a lump or a tightness in the throat. Whether all of these symptoms should be classified under alimentary symptoms as a type of dysphagia is doubtful. Some patients linked this symptom with their shortness of breath, which may point to involvement of the upper respiratory tract.

Colic.

Colic was always accompanied by nausea and/or vomiting. In two cases this symptom was so severe that a primary abdominal lesion was at first suspected.

Frequency of Micturition and/or Diuresis.

Diuresis was more common than frequency of micturition. Frequency of micturition occurred either during the attack or immediately after it. The outstanding feature of the diuresis was its long duration. Only one other symptom outlasted this one, and that was exhaustion. Often the diuresis continued for up to six hours after the acute attack. Evidence that diuresis had occurred in these patients was not based on objective measurements. It was included as a symptom only in those cases in which the author was satisfied that there had been an increased urinary output.

Differential Diagnosis.

Lewis points out that the syndrome presents diverse clinical pictures that often mimic serious organic disease (Lewis, 1954). He says:

Among the original diagnoses he lists: coronary, rheumatic, hypertensive and congenital heart disease; asthma, emphysema, and respiratory tract infection; epilepsy, brain tumour, poliomyelitis, and cerebrovascular accident; "nerves", functional disorders and hyperventilation syndrome (one patient); cardiospasm, peptic ulcer, cholecystitis and cholelithiasis; rheumatoid myositis (fibrositis), myositis and arthritis; islet cell tumour of pancreas, pheochromocytoma, hyperthyroidism, hypothyroidism, insulin reactions and "glands"; and "allergic condition".

This series cannot show such an array of misdiagnoses. Previous diagnoses were as follows: heart lesions, five cases; gastro-intestinal lesions, three cases; epilepsy, two cases; "nerves" (neurosis), five cases; hyperthyroidism, one case. The diagnosis of neurosis is not to be considered as a serious mistake. However, the "medical panorama" of misdiagnoses as presented by Lewis should be heeded as a warning when any of the characteristic symptoms of this syndrome are present.

Ætiology.

In 42 cases a psychological basis for the disease was discovered, and somatic factors were contributory in four cases.

The latter cases are worthy of mention. In two cases the syndrome was a manifestation of the menopause, in another a manifestation of premenstrual tension, and in the fourth case it was associated with dysmenorrhœa. In 11 out of the 42 psychic cases economic hardship was the cause of the stress, and in nine others it was a contributory factor. Other causes of stress varied from an impotent husband to a death in the family. In four cases the pathogenesis was not discovered.

Treatment.

The treatment depends upon whether one is treating an acute episode or being consulted about a previous episode. The treatment of the acute episode depends upon the extent of the agitation of the patient. If the patient is extremely agitated, then explanatory or educational therapy is left for a subsequent consultation. In these cases a sedative is administered (3 to 6 grains of sodium phenobarbitone by intramuscular injection) and the patient is assisted to rebreathe into a plastic bag with the attachments that have been previously described. (Nearly every home possesses a large plastic bag and a length of garden hose.) When patients are amenable to explanation they are treated in the same way as those who consult about a previous episode.

In the treatment of the latter the most important single step is the reduplication of the syndrome by means of voluntary overbreathing. When patients experience the symptoms as a result of complying with the request to overbreathe they are on the way to understanding their complaint. Then, having the attack terminated by the simple procedure of rebreathing into a plastic bag further impresses upon them the relationship between the disordered breathing and their symptoms.

The mechanism of their symptoms can be further explained by the statement that the overbreathing causes the loss of too much carbon dioxide, and that since carbon dioxide is an acid, this loss causes an alkalinity of the blood. This part of the story can be made to suit the patient's standard of education.

At the next visit the patient is asked to bring along another person—spouse or friend. This person is then asked to overbreathe until the characteristic symptoms are induced. If symptoms cannot be induced in this person (and this is rare), then the patient brings along another person at a subsequent visit.

The patient witnesses the appearance of symptoms in a normal person and is told that nearly everyone suffers these self-same symptoms with overbreathing. This serves a double purpose. In the first place the patient is presented with additional evidence that he is not in fact abnormal, and that his condition is merely due to an abnormal amount of normal function. Secondly, if it is the spouse who is the guinea-pig, then often the patient's symptoms are received with much greater understanding in the home. Giving a taste of the discomforts of hyperpnœa is a potent method of arousing sympathy and understanding for the patient.

The patients were instructed to regulate their breathing, but not to the extent of consciously executing each inspiration and expiration. Many attacks were averted by patients holding their breath at the first sign of the heralding symptom. They were told to hold their breath until they could hold it no longer, then to breathe once out and in and to hold it again; they were told to repeat this until they felt absolutely normal. There were a few who could not stop hyperventilating and who would, without some help, go on to either syncope or tetany of the respiratory muscles. For these people, and also for those who became extremely agitated during an attack, the use of the plastic bag was found necessary. These patients were taught how to use the bag by blowing into it and sucking from it. Strict instructions were given that it was not to be used for more than two minutes at a time (because of the depletion of oxygen from it). If its use for more than two minutes was required, the patient was told to squeeze the bag empty and to blow the bag up until it was half-full and then to rebreathe again from and into it. Help was given with regard to psychological problems and sedatives were prescribed when considered necessary. About 45 of the patients showed improvement with this regime.

Discussion.

Bernard I. Lewis has done a lot in America to place the hyperventilation syndrome in its correct perspective. In 1954 he reported a series of 50 cases of this syndrome (Lewis, 1954).

On superficial examination there would appear to be considerable difference between this series and that of Lewis. However, these differences could well be explained by: (i) differences in classification and mode of presentation; (ii) differences in the particular population from which the patients were drawn; and (iii) differences in the technique of eliciting symptoms.

It was Sole and Shock (1938) who first claimed that hyperventilation was responsible for the symptoms of the effort syndrome. Since that time a considerable controversy has raged on this question.

Paul Wood published an authoritative article on the effort syndrome in 1941, and in this article he discarded the view that the symptoms of the effort syndrome were due to hyperventilation (Wood, 1941). Wood listed the symptoms of the effort syndrome and gave the incidence of these symptoms.

In Table II the percentage occurrence of these symptoms in the present series of hyperventilation cases is compared with the percentage occurrence of the same symptoms in Wood's series of effort syndrome cases.

TABLE II.

Symptom.	Percentage of Cases.	
	Wood's Series (200 Cases).	This Series (50 Cases).
Breathlessness	93	86
Palpitations	89	76
Fatigue	88	92
Sweats	80	68
Nervousness	79	88
Dizziness	78·5	—
Pain (left chest)	78	28
Headaches	72·5	32
Trembling	65	94
Sighs	62	82
Flushes	57	66
Throbs	57	—
Cramps	57	18
Paraesthesia	56	48
Dry mouth	55	56
Syncope	34·5	26
Vomiting or diarrhœa	26	38
Insomnia	18·5	—
Frequency of micturition	10·5	32
Anorexia	20	—
Light-headedness	—	90
Giddiness	—	48
Tinnitus	—	36
Blurred vision	—	52
Cold feeling	—	58
Skeletal pain (other than left chest)	—	16
Globus hystericus	—	18
Acrophagy	—	30
Colic (alimentary)	—	12

Wood's cases are preselected by certain symptoms (for example, chest pain) because it would be natural that a big percentage of "cardiac neuroses" would be among his 200 cases. This in itself would account for some difference between the two series. Then the same may be said in comparing the two series as was said when reference was made to Lewis's series. In particular that reason which concerns the mode of presentation of results is very important in this connexion—for example, in this series headache was included only if it occurred during the bout itself. Many patients complained of headache apart from the attacks; but these were not included. It would appear that the effort syndrome also occurs in bouts.

> The symptoms of Da Costa's syndrome are rarely if ever confined to exertion. They may occur at any time during the day or night, and they are invariably provoked by emotion.

Were the headaches in Wood's series entirely confined to the attack itself?

The fact that insomnia and anorexia are among the symptoms listed by Wood suggests that he has included symptoms which were not confined to the acute bout.

When these factors have been taken into consideration it is seen that the symptoms of the effort syndrome and those of the hyperventilation syndrome run suspiciously parallel.

The reasons that Wood advances against the hyperventilation theory for the effort syndrome are as follows: (i) The same symptoms and the same biochemical findings may be induced by forced breathing in controls as in patients with the effort syndrome. (ii) They (Soley and Shock) made no attempt to correlate these phenomena with effort. (iii) Forced breathing before effort increased the capacity for effort in controls (Douglas and Haldane). (iv) Ventilation in excess of the body's needs has not been demonstrated during effort. (v) The plasma bicarbonate level is not reduced in cases of the effort syndrome (Adams and Sturgess, 1919). (vi) The urines of patients with the effort syndrome (17 cases) and of controls (13 cases) demonstrate the normal development of an acid urine during effort.

Let these six points be examined.

The fact that the same symptoms can be induced in normal people is not evidence against the hyperventilation theory of the effort syndrome. It is a well-known fact that these symptoms, which characterize the hyperventilation syndrome, occur (in a varying degree) in all people who hyperventilate. The difference between a person who is suffering from the hyperventilation syndrome and one who is not is that in the former the hyperventilation appears involuntary, whilst in the latter it is produced voluntarily.

The second reason advanced by Wood is that Soley and Shock made no attempt to correlate these phenomena (that is, the symptoms which characterize the effort syndrome) with effort. There was no need for them to do this because the effort syndrome is rarely if ever confined to exertion. The passage to this effect from Wood, already quoted, answers his third and fourth points because it makes relationships with exertion irrelevant.

Wood's fifth point was that the plasma bicarbonate level is not reduced in cases of the effort syndrome (Adams and Sturgis, 1919). Unless the plasma bicarbonate-level investigations were carried out whilst the patient was suffering from symptoms (and there is no suggestion that this was the case—all observations were made on patients at rest and at least eight hours after the last meal), then these findings were irrelevant.

The last reason that was advanced was that the urine of patients with the effort syndrome demonstrated the normal development of an acid urine during effort. Reasons have already been given that the changes during effort in these cases are irrelevant. After effort the 17 patients (those suffering from the effort syndrome), in Wood's own words, "did show a tendency to hyperventilation. The pH of the urine in these cases did rise after effort whilst the pH of the urine in the controls fell". This indicates a respiratory neurosis in these cases, and the experiment, rather than supplying evidence against the hyperventilation theory, has produced results strongly in favour of it. Many patients with the hyperventilation syndrome show this same reaction of lack of apnœa after forced breathing.

The reasons favouring hyperventilation as the cause of the symptoms of the effort syndrome are as follows: Firstly, breathlessness was the most frequent symptom listed by Wood in his series of cases. In fact it occurred in 93% of his cases compared with 85% in the present series. Combine this finding of Wood with the passage from his paper previously quoted. It is apparent that in Wood's series of cases breathlessness often occurs in the absence of exertion. If there is no exertion there is no extra production of carbon dioxide, and if increased pulmonary ventilation occurs at this time alkalosis must result. Other investigators found that breathlessness was a common symptom of the effort syndrome with the following percentage incidence: 97·5% in 40 cases (Parkinson, 1916); 67·5% in 1000 cases (Hume, 1918); 80% in 50 cases (Friedlander and Freyhof, 1918); 100% in 100 cases (Addis and Kerr,

1919); 74% in 90 cases (Swan, 1921); 77% in 50 cases (Craig and White, 1934). Earlier in this paper it was stated that in the case of the hyperventilation syndrome increased pulmonary ventilation did not always reach consciousness; and Lovatt Evans has stated that: "We are not generally aware of an increase in the volume of the pulmonary ventilation until this has been about doubled." In view of this it is possible that increased pulmonary ventilation does occur in all cases of the so-called effort syndrome.

Secondly, the similarity in the symptoms of the two syndromes is significant.

Thirdly, in both syndromes forced breathing induces a sensation of breathlessness; and in both cases hyperventilation frequently replaces apnœa after forced breathing.

Fourthly, the symptoms are invoked by emotional stimuli in both syndromes.

The hyperventilation syndrome is almost certainly restricted to *Homo sapiens*. It is one of the prices that we pay for speech. Pavlov stated: "It is precisely speech which has made us human." The main function of respiration, of course, is to do with gaseous exchange; but in the human it plays a very important role in phonation. In order to play this role the respiratory centre must come under voluntary control. This, of course, must involve the motor centre of speech discovered by Broca. Included in this voluntary control is the susceptibility of the respiratory system to emotional stimuli. Hence the following expressions: sigh with relief; gasp with horror; yawn with tiredness; pant with eagerness or excitement. *Homo sapiens* is certainly a sitting shot for hyperpnœic alkalosis. In man respiration is altered for reasons other than those already mentioned. These are coughing and sneezing and also assistance in the expulsion of the products of the alimentary canal as well as those of the urinary and reproductive systems (Wood Jones, 1941).

Summary.

Fifty cases of the hyperventilation syndrome are presented and its frequency of occurrence in general practice is noted. The diagnosis of this condition is discussed and the symptoms are tabulated and examined. Comparison is made with a similar series of cases recorded by Lewis in 1954. The treatment of this symptom complex is explained. It is pointed out that unless many of the "turns" encountered in medical practice are suspected as being caused by hyperventilation, many mistakes in diagnosis will be made.

Evidence is produced to show that hyperventilation may well produce some or all of the symptoms in some or all of the cases of the effort syndrome.

References.

ADAMS, F. D., and STURGIS, C. C. (1919), "Note on the Vital Capacity of the Lungs and the Carbon Dioxide Combining Capacity of the Blood in Cases of 'Effort Syndrome'", *Amer. J. med. Sci.*, 158: 816.

ADDIS, T., and KERR, W. J. (1919), "The Relative Frequency in Recruits With and Without Thyroid Enlargement of Certain Signs and Symptoms which occur in Neurocirculatory Asthenia", *Arch. intern. Med.*, 23: 316.

CRAIG, H. R., and WHITE, P. D. (1934), "Etiology and Symptoms of Neurocirculatory Asthenia", *Arch. intern. Med.*, 53: 633.

DOUGLAS, C. G., and HALDANE, J. S. (1909), "The Regulation of Normal Breathing", *J. Physiol. (Lond.)*, 38: 420.

EVANS, C. L. (1947), "Principles of Human Physiology", Ninth Edition: 739.

FRIEDLANDER, A., and FREYHOF, W. L. (1918), "Intensive Study of 50 Cases of Neurocirculatory Asthenia", *Arch. intern. Med.*, 22: 693.

HUME, W. E. (1918), "The Studies of Cardiac Disabilities of Soldiers in France", *Lancet*, 1: 529.

JONES, F. WOOD (1941), "The Musculature of the Body Cavities", *J. Chart. Soc. Mass. med. Gymn.*, 27: 54.

KERR, W. J., DALTON, J. W., and GLIEBE, P. A. (1937), "Some Physical Phenomena Associated with the Anxiety States and Their Relation to Hyperventilation", *Ann. intern. Med.*, 11: 961.

LEWIS, B. I. (1954), "Chronic Hyperventilation Syndrome", *J. Amer. med. Ass.*, 155: 1204.

PARKINSON, J. (1916), "Cardiac Disabilities of Soldiers on Active Service", *Lancet*, 2: 133.

PAVLOV, I. (1949), "Complete Works", 111: 336.

SOLEY, M. H., and SHOCK, N. W. (1938), "The Etiology of Effort Syndrome", *Amer. J. med. Sci.*, 196: 840.

SWAN, J. M. (1921), "An Analysis of 90 Cases of Functional Disease in Soldiers", *Arch. intern. Med.*, 28: 586.

WOOD, P. (1941), "Da Costa's Syndrome (or Effort Syndrome)", *Brit. med. J.*, 1: 767.

THE NON-INFECTIVE ARTHRITIDES.[1]

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THE term "arthritides", when used in its widest sense, embraces all forms of chronic arthritis, but in this paper it is used more specifically to connote chronic joint diseases which show evidence of an inflammatory process.

De Witte and his associates (1951) classify the chronic arthritides into (i) arthritis due to infection in which the ætiological agent is known and (ii) chronic arthritis in which the ætiology is either unknown or controversial. It is with this latter group that we shall deal.

The basic lesion of this group of diseases is not yet clearly known, but they are apparently generalized disorders of varied ætiology in which inflammatory and toxic factors play an important role, and which manifest themselves not only in the joints but also in the supporting tissues of the body (Kellgren, 1952; Schinz *et alii*, 1952).

For convenience and on the grounds of clinical, biochemical and radiological differences, we may distinguish the following groups: (i) rheumatoid arthritis; (ii) Still's disease; (iii) Felty's syndrome; (iv) ankylosing spondylitis; (v) psoriatic arthritis; (vi) villonodular synovitis.

Rheumatoid Arthritis.

Rheumatoid arthritis is considered as a systemic disease in which the joint lesions vary greatly, depending on the severity of the disease. Rheumatoid arthritis tends to involve the joints symmetrically, although the condition often starts on the right side. Bilateral involvement of multiple joints is the rule, the small joints of the hands and feet being mainly affected. The larger joints of the extremities and the spinal joints may also be involved. In some cases the lesion, instead of being a symmetrical polyarthritis, is confined to a single joint. In the monarticular lesion the affected joint is commonly the wrist joint, but it may be a hip, knee, ankle, tarsal, temporo-mandibular or sterno-clavicular joint.

At the other extreme there are cases in which all, or nearly all, the joints of the body are affected, including the terminal interphalangeal, sacro-iliac and spinal joints (Simon, 1960).

Early in the disease there occurs proliferation of the synovial cells, thickening of the synovial membrane, effusion into the joint and periarticular soft-tissue swelling. As the disease progresses, pannus invades and destroys the cartilage and subchondral bone, causing apparent narrowing of the joint space, erosions of the articular ends of the bones and subchondral cyst or pseudo-cyst formation. Atrophy of bone accompanies these changes, and in a survey of 532 cases carried out by the Scientific Advisory Committee of the Empire Rheumatism Council (1950), diminished density was found in 93% of cases, while marked thinning of the trabeculæ and thinning of the cortex were often seen. These changes, which are so characteristic of early and

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on November 24, 1960.

moderately advanced arthritis, are classically seen in the hands and feet, where the proximal interphalangeal and the metacarpo- and metatarso-phalangeal joints are mainly affected. The periarticular swelling, apparent narrowing of the joint spaces and demineralization of bone adjacent to the joints are well known to us all, but the marginal destructive changes involving the articular cortex and subchondral bone which are so characteristic of rheumatoid arthritis are worthy of further consideration.

Fletcher and Rowley (1952) classify bone erosions into surface erosions confined to the cortex, pocketed erosions involving cortex and spongiosa, and enclosed erosions confined to the spongiosa, the latter being the cystic or pseudo-cystic areas of the older writers. Early erosions may appear as no more than a slight break in the continuity of the articular cortex, but more commonly they appear as half-moon erosions measuring 2 to 5 mm., either of the articular cortex or juxta-articular margins. At times the destructive changes resemble the punched-out areas of destruction found in osteochondritis dissecans and gout, and differentiation from gout on the radiological changes alone may be impossible. Enclosed erosions confined to the spongiosa appear as small circular translucencies which may lie several millimetres from the joint surface. These erosions are identical in appearance with the subchondral cyst formation of osteoarthritis. Occasionally they may be very large, measuring a centimetre or more in diameter, and may simulate exactly the translucent zone caused by a urate deposit in gout. The most frequent sites for articular or marginal erosions, which may be single or multiple, are the tip or either side of the ulnar styloid, the edges of the second and third metacarpal heads and the bases of the proximal phalanges, which may become splayed out to produce a cup-like deformity. In the knee, erosions are found on the lateral and medial margins of the tibia, and they are also common in the heads of the metatarsals.

As the disease progresses, retractive processes involving the capsular apparatus produce subluxations, dislocations and contractural deformities. These changes are best seen in the hands, where there is subluxation of the metacarpo-phalangeal joints and ulnar deviation of the fingers, but deformities are not confined to the hands and feet and are commonly found in the larger joints of the extremities.

With rheumatoid arthritis of long standing, a high degree of disuse osteoporosis may be found, transforming bones into slender rods.

Occasionally, instead of osteoporosis there is found an endosteal increase in bone density. Endosteal sclerosis especially attacks the terminal and middle phalanges of the hands and the distal parts of the femoral and proximal parts of the humeral shafts. Keats (1958) points out that the endosteal plaques are too distant from the articular surfaces to suggest a relationship to ingrowth of granulation tissue and suggests that they may be areas of infarction caused by vascular disturbances secondary to the inflammatory process present in the joint.

When rheumatoid disease is advanced articular destruction may produce a complete obliteration of the joint spaces and fibrous or bony ankylosis ensues. Not infrequently extensive resorption takes place in the articular surface of bones forming the joint, and destruction of articular and subarticular bone may be so profound as to give the impression of either excision or resorption of the entire articulating portion of the joint. These changes, which may have been termed arthritis mutilans, are most frequently encountered in *la main en lorgnette* or opera-glass hand. Trophoneuritic disturbances probably play a part in the production of the severe mutilations, hence the similarity of these changes, particularly at the elbow, shoulder and knee joints, to the Charcot's joints of a neurogenic arthropathy.

Differential Considerations.

Radiography may be of help in difficult cases and in the differentiation between similar diseases in the early stages.

Differentiation between gout and rheumatoid arthritis can occasionaly present a radiological diagnostic problem. Usually the clinical findings of an abrupt onset, periodic elevation of blood uric acid levels, a clinical response to colchicine and radiological findings of articular and subarticular cystic defects associated with tophaceous deposits in the soft tissues help to make the diagnosis. In gout osteoporosis is not a feature.

Osteoarthritis may simulate the quiescent stage of rheumatoid arthritis. In the hand, involvement of the terminal interphalangeal is found rather than the proximal interphalangeal joints, which are characteristically involved in rheumatoid arthritis. Periarticular and intraarticular swellings are not featured in osteoarthritis, and there is only very little deossification of nearby bones. Fibrous or bony ankylosis does not occur.

Davis *et alii* (1957) review cases of multiple myeloma in which deposits of amyloid occur and are associated with swelling, pain and limitation of movement of adjacent joints. This picture can lead to a clinical diagnosis of rheumatoid arthritis.

In disseminated lupus erythematosus the exact pattern of rheumatoid arthritis may be duplicated, but the radiological pattern mimics the early stages only of rheumatoid disease. The characteristic radiological feature of the arthritis of disseminated lupus erythematosus is the absence of erosion or joint-space narrowing in the presence of deformities and osteoporosis (Vaughan, 1958).

In acromegaly the most frequent abnormality found in 26 patients (Steinbach *et alii*, 1959) was a marked thickening of the soft tissues of the fingers and toes. The thickening is particularly prominent about the proximal interphalangeal joint of fingers because of the involvement of the joint capsule and synovial lining producing a fusiform shape similar to that seen in rheumatoid arthritis.

Still's Disease (Juvenile Rheumatoid Arthritis).

Still's disease is a general systemic condition of which rheumatoid arthritis is merely one of the manifestations (Lodge, 1955). The chief incidence is between 2 and 5 years of age, with a preponderance of females over males. Monarticular and polyarticular forms are described, the hands, wrists, feet, ankles and knees being mainly involved. The spine may be affected, the cervical apophyseal joints being involved much more frequently than in adults. In the acute presentation, rashes, pyrexia, leucocytosis, cardiac involvement and enlargement of reticulo-endothelial tissues — that is, splenomegaly, heptomegaly and lymphadenopathy — are associated with changes in the joints. A chronic form of slow and insidious onset produces symptoms mainly referable to the joints, as in adults.

Often the first radiological sign is a periosteal reaction along the shaft of a metacarpal or metatarsal bone, with early changes in the adjacent joints. Osteoporosis, apparent loss of joint space due to destruction of articular cartilage, bone erosions, subluxations and ankyloses are sequelæ which follow closely the manifestations of adult rheumatoid arthritis.

As a result of hyperæmic changes around the growing ends of bones, disturbances of bone growth are frequently encountered. Accelerated epiphyseal growth produces elongated configurations of the long bones and tapering of the juxtaepiphyseal parts of the shafts, while different rates of growth and premature fusion of the epiphyses may result in gross deformities in paired or adjacent bones (Middlemiss, 1951).

Felty's Syndrome.

In 1924 Felty described cases of chronic rheumatoid arthritis associated with splenomegaly and leukopenia. There is little evidence to suggest that this is more than a minor variant of rheumatoid arthritis, although recent reports have suggested that a proportion of cases are probably examples of disseminated lupus erythematosus.

Ankylosing Spondylitis.

The pathological changes in the diarthrodial joints in ankylosing spondylitis resemble closely those of rheumatoid arthritis, but the two diseases differ in important respects and are considered in Great Britain to be separate diseases representing a common reaction to different ætiological factors (Cruickshank, 1951).

Primarily the disease is destructive, with osteoporosis and bone destruction being followed by a reparative phase with bone reaction and bone production. The tissues involved are primarily connective tissue and the sites mainly involved are the sacro-iliac joints and the joints and ligaments of the spine. The earliest changes are found in the sacro-iliac joints, in which there is slight widening of the joint space with erosions of the articular cortex and blurring of the adjacent trabeculæ. These changes, which are best seen in the lower third of the joint, are usualy bilateral, but may be unilateral.

Differentiation of these changes must be made from those found in normal people between 18 and 24 years. West (1949) criticizes the use of the expressions "lack of definition", "ground-glass appearance" and "haziness" as descriptive terms of early ankylosing spondylitis on the grounds of having found such appearances in the sacro-iliac joints of 40 allegedly normal university students.

With progression of the disease, the sacro-iliac joint space narrows and becomes obliterated, sclerosis develops on both sides of the joint and bony ankylosis occurs. Occasionally sclerosis may be a very marked feature and differentiation has to be made from Paget's disease, osteoblastic secondaries and osteitis condensans ilii, in which the sclerosis is strictly confined to the iliac bones. The earliest changes in the spine are postural, with loss of the normal lumbar lordosis. The earliest local changes are in apophyseal joints, which become blurred and eventually obliterated, while the costo-vertebral and costo-transverse joints are similarly affected.

With further progression of the disease, the vertebral bodies lose their trabecular pattern and show a ground-glass appearance. They also lose their normally rounded upper and lower anterior margins, and the concave anterior contour becomes straightened, so that the bodies become "squared" and present a "box-like" aspect in the lateral projection.

A rare complication of ankylosing spondylitis is the destructive change involving the intervertebral disks and adjacent vertebral bodies, which, though closely resembling the changes of tuberculosis, brucellosis or a pyogenic condition, constitute another manifestation of ankylosing spondylitis.

Wholey, Pugh and Bickel (1960) describe 10 cases in which the lesions, all in males, were mainly in the thoraco-lumbar region and involving two contiguous vertebræ. Early destruction was soon followed by osteosclerosis, indicating an active process, and biopsies showed inflammatory tissue typical of a rheumatoid lesion.

An occasional complication is vertebral subluxation, and this most commonly occurs in the cervical region.

To help protect the spine's stability after the joints have become affected, calcification develops in the paraspinal ligaments and may be discerned as a faint, hair-like shadow joining the vertebral bodies in the thoraco-lumbar region. As the disease becomes advanced and the final stage of repair and healing by ossification is reached, the bodies become united by dense, narrow lines of calcified tissue and the classical "bamboo spine" results. These lines of calcified tissue are narrow, and project less laterally or anteriorly than the complete bony bridging seen secondary to disc degeneration.

The peripheral joints and connective tissues may also be affected in ankylosing spondylitis.

Calcification, followed by ossification, takes place in connective-tissue planes and may be found in the ilio-lumbar ligaments, the pelvic muscles and the adductor muscles of the thigh and around the calcaneus at the attachments of the tendo Achillis and long plantar ligaments. A painful heel may be an early and important presenting symptom.

The joint changes, mainly in the hips, shoulders, hands and feet, are similar to those of rheumatoid arthritis, but the over-all picture differs. Generalized osteoporosis is usually absent, ulnar deviation or varus deformity rarely occurs and destruction of the articular cortices is found more at joint margins and progresses away from the joints rather than towards the articular cartilages (Middlemiss, 1956).

Psoriatic Arthritis.

It is debatable whether psoriatic arthritis is a distinct entity or merely the coexistence of two diseases.

The radiographic changes in psoriatic arthritis are those of an atrophic arthritis without marked osteoporosis. These changes are associated with pitting or roughening of the nails of the affected digits.

The earliest changes are marginal erosions of the articular ends of the phalanges. Irregular areas of destruction develop and extend along the shafts of the bones, imparting a scalloped appearance to the cortex with numerous punched-out defects. Occasionally there is bone proliferation at the margins of the destroyed joint with periarticular calcification, so that differentiation from gout may be difficult. Changes are also found in the terminal phalanges, in which there is overgrowth at the tendon insertions, causing marginal splaying of the bases and erosions of their tips so that an "inverted golf-tee" appearance is produced. The erosions which start as cystic areas in the ungual tufts are often well shown in the terminal phalanx of the big toe.

At a later stage there may be gross destruction of the distal ends of the phalanges, giving rise to "spindle" or "thorn types" of phalanges which have a fairly characteristic appearance, although reminiscent of the destructive lesions of syringomyelia.

Attention has been drawn to the relatively high incidence of ankylosing spondylitis in patients with psoriatic arthritis. Wright (1957), reviewing 39 cases of psoriatic arthritis, noted that three patients had clinical ankylosing spondylitis while 20% of the group had radiological evidence of bilateral changes in the sacro-iliac joints which varied from articular erosions and juxta-articular sclerosis to partial or complete ankylosis.

Villonodular Synovitis.

This disease was previously known as xanthoma or synovial giant cell tumour. The term "villonodular synovitis" was coined by Jaffe *et alii* (1941) to describe nodular, soft-tissue masses arising from tendon sheaths and joint synovia. They concluded from their studies that the lesion is an inflammatory rather than a neoplastic process.

The lesions may be circumscribed or diffuse, with the synovial membrane generally thickened, pigmented and covered with villous and coarse nodular outgrowths. It is with the diffuse form that bone lesions are associated.

Microscopically the lesions show pronounced vascular development, inflammatory infiltration and marshalling of phagocytes. The latter accumulate hæmosiderin from broken-down blood products, and if large numbers of hæmosiderin-containing cells are present, the mass is dark in colour and termed pigmented villonodular synovitis.

The disease, which is usually monarticular, has been described in the hip, knee, ankle, elbow and wrist joints and in the tendon sheaths of the fingers. Huge swelling of the capsular soft parts may be the only radiological finding, the soft-tissue swelling showing density in accordance with the hæmosiderin content. Bone lesions appear at the involved joint as sharply circumscribed erosions and single or multiple cysts having thin sclerotic margins. Although there are numerous other diseases in which bone erosions are seen in conjunction with soft tissue masses, erosions and single or multiple cysts in bone adjacent to an articular surface with a noncalcified lobulated intra-articular mass, normal bone mineralization and preservation of the joint space appear to be characteristic of villonodular synovitis (Breimer and Freiberger, 1958).

References.

BREIMER, C. W., and FREIBERGER, R. H. (1958), "Bone Lesions Associated with Villonodular Synovitis", *Amer. J. Roentgenol.*, 79: 618.

CRUICKSHANK, B. (1951), "Histopathology of Diarthrodial Joints in Ankylosing Spondylitis", *Ann. rheum. Dis.*, 10: 393.

DAVIS, J. S., WEBER, F. C., and BARTFELD, H. (1957), "Conditions Involving the Hemopoietic System Resulting in a Pseudorheumatoid Arthritis; Similarity of Multiple Myeloma and Rheumatoid Arthritis", *Ann. intern. Med.*, 47: 10.

FLETCHER, D. E., and ROWLEY, K. A. (1952), "The Radiological Features of Rheumatoid Arthritis", *Brit. J. Radiol.*, 25: 282.

JAFFE, H. L., LICHTENSTEIN, L., and SUTRO, C. J. (1941), "Pigmented Villonodular Synovitis, Bursitis, and Tenosynovitis", *Arch. Path. (Chicago)*, 31: 731.

KEATS, T. E. (1958), "Two Unusual Manifestations of Advanced Rheumatoid Arthritis", *Radiology*, 71: 735.

KELLGREN, J. H., BALL, J., and TUTTON, G. K. (1952), "The Articular and Other Limb Changes in Acromegaly; Clinical and Pathological Study of 25 Cases", *Quart. J. Med.*, 21: 405.

KELLGREN, J. H. (1952), "Concepts of Rheumatic Disease', *Brit. med. J.*, 1: 1093.

KELLGREN, J. H. (1952), "Concepts of Rheumatic Disease", *Brit. med. J.*, 1: 1152.

LODGE, T. (1955), "Recent Advances in Radiology", Churchill, London: 64.

MIDDLEMISS, J. H. (1951), "Juvenile Rheumatoid Arthritis (Still's Disease)", *Proc. roy. Soc. Med.*, 44: 805.

MIDDLEMISS, J. H. (1956), "Ankylosing Spondylitis", *J. Fac. Radiol. (London)*, 7: 155.

SCHINZ, H. R., BAENSCH, W. E., FRIEDL, E., and UEHLINGER, E. (1952), "Roentgen Diagnostics", Grune and Stratton, New York, 2: 1368.

SCIENTIFIC ADVISORY COMMITTEE (EMPIRE RHEUMATISM COUNCIL) (1950), "A Controlled Investigation into the Ætiology and Clinical Features of Rheumatoid Arthritis", *Brit. med. J.*, 1: 799.

SIMON, G. (1960), "Principles of Bone Xray Diagnosis", Butterworth, London: 149.

STEINBACH, H. L., FELDMAN, R., and GOLDBERG, M. B. (1959), "Acromegaly", *Radiology*, 72: 535.

VAUGHAN, B. F. (1958), "The Radiological Aspects of Collagen Disease", *Proc. Coll. Radiol. (Aust.)*, 2: 11.

WEST, H. F. (1949), "The Ætiology of Ankylosing Spondylitis", *Ann. rheum. Dis.*, 8: 143.

WHOLEY, M. H., PUGH, D. G., and BICKEL, W. H. (1960), "Localised Destructive Lesions in Rheumatoid Spondylitis", *Radiology*, 74: 54.

WITTE, F. DE, BEYLEN, C. VAN, and THYS, L. (1951), *"Le lésion articulaires chroniques non le traumatiques"*, *J. Radiol. Electrol.*, 32: 226.

WRIGHT, V. (1957), "Psoriasis and Arthritis: A Study of the Radiographic Appearances", *Brit. J. Radiol.*, 30: 113.

OBSERVATIONS ON MEGALOBLASTIC ANÆMIA OF PREGNANCY IN PAPUA.

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IT has been recognized for some time that severe anæmia is a common complication of pregnancy in New Guinea; but as far as is known, no investigation has been carried out to determine the incidence of megaloblastic anæmia in pregnancy and the puerperium. For this reason, it was decided to conduct a survey on patients admitted to the obstetrical department of the General Hospital, Port Moresby, over a period of six months, commencing on April 14, 1960.

It was appreciated that there were many factors limiting the value of such an investigation. The General Hospital caters for the population of Port Moresby and surrounding areas, and it also acts as a receiving centre for complicated cases from more remote districts. Also the population of the town itself is not homogeneous, but contains representatives of most of the mainland tribes, as well as some from the neighbouring islands. More important than these factors is the aversion of most of the native women to enter hospital for confinement. When they do so, they are often seen for the first time by a doctor during or shortly after labour, and are not willing to remain in hospital for more than a few days. It is also exceedingly difficult to persuade them to return for investigation or treatment as out-patients. It was obvious that under these conditions it was necessary to establish the diagnosis as quickly and accurately as possible.

Foy *et alii* (1952) have shown that a megaloblastic anæmia can exist that is not macrocytic, and a macrocytic anæmia that is not megaloblastic, and they refer also to microcytic and normocytic anæmias in which the marrow shows definite evidence of megaloblastic hyperplasia. In the same year Kothari and Bhende reviewed 100 cases of megaloblastic anæmia of pregnancy in India, and showed that the red cells in the blood could be macrocytic, normocytic or microcytic, and hyperchromic or hypochromic. In a preliminary report in 1949 they had demonstrated that there were no specific signs and symptoms, and that the only reliable criterion for the diagnosis of the condition was the presence of megaloblasts in the marrow or peripheral blood. As these cells are not always present in the blood, and are more easily found in the marrow, obviously the most satisfactory method is the examination of marrow smears.

As it was not practicable to subject every anæmic patient to sternal puncture, only those with a hæmoglobin level of 8 grammes per 100 ml. or less were investigated. It was realized that this method would not disclose all cases, as iron deficiency may be so severe as to prevent the development of the megaloblastic component until iron is given (Tasker *et alii*, 1956), and megaloblastic anæmia may exist with a hæmoglobin level higher than 8 grammes per 100 ml.

In this series, all patients except two were given iron, usually in the form of "Imferon", as soon as the hæmoglobin level was shown to be below 10 grammes per 100 ml., and folic acid (10 mg. three times a day) also, if it was below eight grammes per 100 ml. Treatment with the latter was not commenced until sternal puncture had been done. Only one patient was transfused.

During the period of the investigation there were 301 confinements, and 13 patients were diagnosed by marrow examinations as suffering from megaloblastic anæmia. Of these, five had two sternal punctures.

Summary of Clinical and Laboratory Findings.

CASE I.—A., a native of Kerema, aged 20 years, pregnant for the second time, was found to have anæmia during pregnancy, when she was also found to be suffering from pyelitis. She had hepatosplenomegaly, and examination of her blood showed the hæmoglobin value to be 3·3 grammes per 100 ml. and the anæmia to be normocytic hypochromic. In her bone marrow mixed normoblastic and megaloblastic erythropoiesis was present. She was treated by transfusion, iron given parenterally and folic acid. At delivery, on June 9, 1960, her hæmoglobin value was 12 grammes per 100 ml.

CASE II.—B., a native of Kerema, aged 32 years, pregnant for the third time, was diagnosed as anæmic during the puerperium, on April 26, 1960. She had suffered from a post-partum hæmorrhage and had hepatosplenomegaly. Examination of her blood showed a hæmoglobin value of 4 grammes per 100 ml., a microcytic hypochromic anæmia. In her bone marrow mixed normoblastic and

megaloblastic erythropoiesis was present. No treatment was given, as the patient absconded. She was seen again on July 13, when her hæmoglobin value was 10 grammes per 100 ml., and she was discovered to have a mild hookworm infestation.

CASE III.—C., a native of Kerema, aged 27 years, pregnant for the third time, was diagnosed as anæmic on May 11, 1960, during the puerperium. She had a hæmoglobin value of 3·8 grammes per 100 ml., and a macrocytic anæmia with a megaloblastic marrow. Hepatosplenomegaly was present and she was also discovered to have a mild hookworm infestation and to be suffering from puerperal sepsis. Treatment with "Imferon" and folic acid was given for one week. On August 30, her hæmoglobin value was 8 grammes per 100 ml., but megaloblasts were still present in her marrow. Treatment with folic acid raised her hæmoglobin value to 10·5 grammes per 100 ml. on October 17, and at this time sternal marrow examination showed normoblastic erythropoiesis.

CASE IV.—D., a native of Kerema, aged 30 years, pregnant for the third time, was diagnosed as anæmic during the puerperium on April 22, 1960, when she was suffering from puerperal sepsis. She had a moderately heavy hookworm infestation also. Her hæmoglobin value was 3·8 grammes per 100 ml., and she had a macrocytic anæmia, with mixed normoblastic and megaloblastic marrow. Treatment with iron by injection was given for one week, and her hæmoglobin value was then 4·3 grammes per 100 ml. She absconded before further treatment could be given. Hepatosplenomegaly was present when she was first examined.

CASE V.—E., a native of Kerema, aged 37 years, pregnant for the seventh time, was diagnosed as anæmic on May 10, 1960, during pregnancy. She had hepatosplenomegaly, and her hæmoglobin value was 7·8 grammes per 100 ml. The anæmia was macrocytic, and the bone marrow showed megaloblastic erythropoiesis. Mild hookworm infestation was present. Treatment with "Imferon" and with folic acid by mouth was given for one month; this was followed by 15 mg. of folic acid given intramuscularly for two weeks. Examination of her sternal marrow at this time still showed megaloblastic erythropoiesis, and her hæmoglobin value was 8·5 grammes per 100 ml. The serum vitamin B_{12} estimation gave a normal result. She absconded at this time. She had mild toxæmia of pregnancy when first examined, and gave a history of having five stillborn children.

CASE VI.—F., a native of Kerema, aged 34 years, pregnant for the seventh time, was diagnosed as anæmic on June 25, 1960, during pregnancy. Hepatosplenomegaly was present. Her hæmoglobin value was 3·1 grammes per 100 ml., and she had a macrocytic anæmia and megaloblastic marrow. Her serum vitamin B_{12} content was normal. A reticulocytosis of 8% was present after one week's treatment with folic acid given by mouth, and the hæmoglobin value was 4·3 grammes per 100 ml. She then absconded.

CASE VII.—G., a native of Kikori, aged 27 years, pregnant for the second time, was diagnosed as anæmic on July 4, 1960, during pregnancy, when she was suffering from a threatened abortion. Her hæmoglobin value was 5·7 grammes per 100 ml., and she had a hypochromic normocytic anæmia with mixed normoblastic and megaloblastic marrow. No treatment was given, as she absconded. *Plasmodium falciparum* was noted in her blood smear at this time. She was delivered on September 22, and her hæmoglobin value at that time was 12 grammes per 100 ml.

CASE VIII.—H., a native of Kerema, aged 28 years, was diagnosed as anæmic on August 9, 1960, during the puerperium. She had an enlarged liver and spleen, her hæmoglobin value was 8 grammes per 100 ml., and a macrocytic anæmia with megaloblastic marrow was found. No treatment was given.

CASE IX.—I., a native of Kerema, aged 28 years, pregnant for the fourth time (twin pregnancy), was diagnosed as anæmic on August 16, 1960, during the puerperium. The liver and spleen were not enlarged. Her hæmoglobin value was 7·8 grammes per 100 ml., and she had a hypochromic microcytic anæmia. Her bone marrow showed mixed megaloblastic and normoblastic erythropoiesis. After treatment with iron and folic acid given orally and parenterally for one month, her hæmoglobin value was 9 grammes per 100 ml., but her marrow showed only normoblasts.

CASE X.—J., a native of Kerema, aged 30 years, pregnant for the fifth time, was diagnosed as anæmic during pregnancy. Hepatosplenomegaly was noted, and her hæmoglobin value was 8 grammes per 100 ml. A macrocytic anæmia and a mixed megaloblastic and normoblastic marrow were present. After treatment with iron and folic acid for two weeks, her hæmoglobin value was 9·8 grammes per 100 ml.

CASE XI.—K., a native of Port Moresby, aged 29 years, pregnant for the seventh time, was diagnosed as anæmic on September 15, 1960, during the puerperium. Her liver and spleen were not enlarged. The hæmoglobin value was 5·5 grammes per 100 ml., and a microcytic hypochromic anæmia was present with a mixed megaloblastic and normoblastic marrow. After treatment for five weeks with iron, folic acid and vitamin B_{12}, sternal marrow examination showed normoblastic erythropoiesis; but her hæmoglobin value was only 7·5 grammes per 100 ml., and remained at this level for another three weeks. She was known to have an "inactive" tuberculosis lesion in one lung.

CASE XII.—L., a native of Kerema, aged 20 years, pregnant for the second time, was diagnosed as anæmic on September 5, 1960, during pregnancy. Hepatosplenomegaly was pronounced. The hæmoglobin value was 5·5 grammes per 100 ml., and a macrocytic anæmia with megaloblastic marrow was present. Iron and folic acid given for two weeks produced no improvement; but three weeks later her hæmoglobin value had risen to 7·5 grammes per 100 ml. A premature stillborn fœtus was delivered at this time. A further examination of her sternal marrow showed only normoblastic erythropoiesis. Examination of her peripheral blood at this time showed gross morphological abnormalities suggestive of hæmolytic anæmia. She was also found to be suffering from a mild hookworm infestation.

CASE XIII.—M., a native of Port Moresby, aged 24 years, pregnant for the seventh time, was diagnosed as anæmic on September 15, 1960, during the puerperium, when she was suffering from puerperal sepsis. Hepatosplenomegaly was present. Her anæmia was of the macrocytic type, and her marrow showed megaloblastic erythropoiesis. Treatment with iron and folic acid raised her hæmoglobin value steadily, so that after five weeks it was 12·5 grammes per 100 ml.

The ages of all the patients in this series were only estimated, as there was no way of discovering their true age. In only two cases was there any history of digestive upset and anorexia. No one complained of a sore tongue. Only two patients were overweight, and six appeared to be undernourished. The livers and spleens were more enlarged than in non-anæmic patients, but not more so than in other women suffering from severe iron-deficiency anæmia.

The diet in all cases was grossly deficient in protein by European standards, and also in green vegetables. It was not possible to discover whether it was inferior to that enjoyed by non-anæmic women.

It was possible to measure the gastric acidity in only two cases, as no patient would submit to gastric intubation, and "Diagnex" was not available until late in the course of the investigation. The fæces were examined for hookworm in only five cases; four of these patients were passing a few ova in their stools, and one a moderately large number.

No increase in fœtal hæmoglobin was found in five cases in which this estimation was made. Also there was no evidence of any abnormal hæmoglobin present.

Discussion.

Megaloblastic anæmia of pregnancy and the puerperium has been known for over 100 years, but until recently has been regarded as a relatively uncommon disease in Europe. However, 14 cases were reported at the Rotunda Hospital, Dublin, in one year by Lillie *et alii* (1954), an incidence of one in 288 pregnancies. Forshaw *et alii* (1957) reported an incidence of about one in 190 hospital confinements at Whiston Hospital. Giles and Shuttleworth (1958) reported a series of 83 cases at the City General Hospital, Stoke-on-Trent, an incidence of one in 39 confinements. In their series all patients with a hæmoglobin value of less than 65% after the thirty-second week were submitted to sternal puncture. It is difficult to believe that diet and conditions of life would differ greatly in Dublin, Liverpool

and Stoke-on-Trent, so that it might be thought that the reported incidence of the disease in temperate climates depends on the intensity of the search made for it. However, it is possible that there are specific geographical loci of the disease, or that people from a certain area may be especially susceptible to it. This is suggested by the series presented here, in which 10 patients were natives of the Kerema area, although only 33 natives of this district were admitted during the period of survey. Of the three remaining patients one was from Kikori, a neighbouring area. The two left (Cases XI and XIII) came from Port Moresby; and the first of these (Case XI) is known to have pulmonary tuberculosis, although this appears to be quiescent at present. Her anæmic condition has failed to improve substantially in spite of all treatment, although her marrow has reverted to normoblastic erythropoiesis. It is difficult to escape the conclusion that this infection may have some bearing on her refractory state.

Various theories have been elaborated to explain the onset of megaloblastic anæmia in pregnancy. Strauss and Castle (1933) suggested that it was due to a temporary reduction in the secretion of intrinsic factor. If this was so, it would be expected that vitamin B_{12} given parenterally should bring about a remission; but usually this does not occur unless massive doses are used. This was shown by Moore, Lillie and Gatenby (1955), who used doses of the order of several thousand microgrammes. It has also been suggested that there may be an underlying steatorrhœa, and three cases of defective fat absorption have been described by Davidson (1948), by Tuck and Whittaker (1950) and by Thompson and Ungley (1951). Badenoch *et alii* (1955), describing nine cases of megaloblastic anæmia of pregnancy, did not demonstrate any abnormality in the secretion of intrinsic factor or in the absorption of fat. They were of the opinion that the anæmia was due to resistance to the action of hæmatopoietic factors, rather than to deficiency. It should be stressed that these investigations refer to European cases and are not necessarily valid for tropical countries. Vitamin B_{12} deficiency in the diet rarely occurs in Europe, whereas Das Gupta (1954) has shown that this deficiency is not uncommon in India. It is also worth remembering that Das Gupta *et alii* (1954) have shown that folic acid by itself is often not sufficient to correct megaloblastic anæmia of pregnancy in tropical countries and that vitamin B_{12} may also be necessary. However, the patient in Case XI was treated with massive doses of B_{12} in addition to folic acid with no effect; but as suggested previously, this may have been due to tuberculosis. It has been suggested that protein deficiency of itself may be a factor in the production of this anæmia in the tropics; but Schofield (1957) could not demonstrate any hæmatological response when a protein dietary supplement was given to pregnant women in Gambia. Although anæmia is known to occur in protein deficiency states such as kwashiorkor, and to be relieved when the condition is alleviated by the addition of protein to the diet, this need only mean that the deficiency must be gross to produce anæmia. Schofield also suggested that there was a hæmolytic factor which ceased directly on delivery, and in the production of which past malarial infection could be suspected of playing a part. Only one patient in this series was shown to be suffering from malaria (Case VII), but it is reasonably certain that all would have suffered from it at one time or another. Many others have noted the occurrence of excess hæmolysis in this anæmia, including Fairley *et alii* (1938), Callender (1944), and Thompson and Ungley (1951). In this series, only one patient (Case XII) showed signs of excess hæmolysis, and she may be suffering from associated congenital hæmolytic anæmia.

Obviously, then, many of the factors which apply in other tropical areas should be important in New Guinea. As has already been noted, there is a deficiency of meat in the diet, and while this may not be a direct cause of megaloblastic anæmia, it is known that the richest animal source of folic acid is liver. When to this meat deficiency is added a deficiency of green vegetables, the main vegetable source of this substance, the combined lack is probably of some importance. It has already been noted that megaloblastic anæmia of pregnancy, while occurring at the rate of one in 23 confinements overall, has an incidence of one in 3·3 in women coming to hospital in Port Moresby from the Kerema district. These people are immigrants to the Port Moresby area, and naturally form a poorer class of the Moresby population. The incidence of malaria and hookworm is higher in them than in the local population. In addition, they have not had time to adjust themselves to a European style of diet as have many of the local population, and in fact cannot afford it. It is also known that hæmolytic anæmia is more common amongst them (unpublished observations). In fact, only two cases of megaloblastic anæmia of pregnancy have been diagnosed in the local native-born population. It would obviously be of importance to know whether this anæmia is equally prevalent amongst women actually living in Kerema at present, or whether it makes its appearance only after their arrival here.

With regard to the effect of folic acid on megaloblastic anæmia in New Guinea, it has been known for some time that this is not effective to the same extent as in European communities. Obviously it will be difficult to obtain accurate figures, because of local conditions. Unfortunately, it was not realized at the time of conducting the survey that some patients with heavy hookworm infestation showed a decrease of serum vitamin B_{12} content as compared with normal subjects (Layrisse *et alii*, 1959), or an effort would have been made to investigate the problem here. All that can be definitely stated in this regard is that of the five patients examined for hookworm, four showed a slight and one a moderate infestation. Of the six patients whose serum vitamin B_{12} level was measured, all were normal, but only one had hookworm infestation. It would thus appear that vitamin B_{12} deficiency is not a serious cause of megaloblastic anæmia in this series.

If megaloblastic anæmia of pregnancy was due purely to a dietary deficiency, it would be expected that a similar anæmia would be found in children in this area. This would seem particularly likely to occur in New Guinea, as it is probable that a combination of deficient diet and infections such as gastro-enteritis is the cause of this anæmia in children (Luhby, 1959), and both these conditions are widespread here. However, about 50 anæmic children were subjected to marrow puncture over the last eight months and no case of megaloblastic anæmia was discovered. Also a better response to folic acid therapy would have been expected among these women. In fact, only five patients did reach a hæmoglobin value of 10 grammes per 100 ml. or more, and two of these received no treatment but appeared to have spontaneous remissions, and one other was transfused. As this investigation was conducted during the "drier" months of the year, a seasonal effect cannot be excluded. Thompson (1952) did produce evidence that there was a higher incidence in England in the winter months, but this has not been confirmed. As far as I am aware, no seasonal variation has been found in tropical countries.

The type of anæmia as disclosed by examination of peripheral blood films was as follows: normocytic and hypochromic, one case; microcytic and hypochromic, four cases; macrocytic, 8 cases. This is perhaps a higher incidence of microcytic hypochromic anæmia than is to be expected, but supports the view that in this country there is probably a multiple dietary deficiency or other factors to be considered. This is also suggested by the fact that four out of five "repeat" marrow punctures showed a reversion to normoblastic erythropoiesis, without a significant increase in the hæmoblobin content of the blood. Gastric acidity in the two cases in which it was estimated (Cases XII and XIII) was normal.

Summary.

An investigation of the incidence of megaloblastic anæmia of pregnancy was conducted at the General Hospital, Port Moresby, during six months commencing April, 1960. During this period 292 confinements took

place, and 13 cases of megaloblastic anæmia were diagnosed, six during pregnancy and seven during the puerperium. Ten of these patients were natives of the Kerema district, although only 33 women from Kerema were admitted to the hospital during the period of the survey. Most of them were recent arrivals to the Port Moresby area.

The response to folic acid therapy was disappointing. There are grounds for supposing that there may be a dietary basis for the condition, but it is suggested that other, at present unknown, factors are also involved. A variable seasonal incidence could not be excluded. There were three cases of puerperal sepsis, one case of pyelitis of pregnancy, one case of toxæmia, one case of antepartum hæmorrhage followed by a still-birth, one case of threatened miscarriage, one case of post-partum hæmorrhage, and one set of twins, amongst the 12 cases reported. This appears to be a high incidence of complications, but it is not considered that valid conclusions can be drawn from such a small series.

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References.

BADENOCH, J., CALLENDER, S. T., EVANS, J. R., TURNBULL, A. L., and WILTS, L. J. (1955), "Megaloblastic Anæmia of Pregnancy and the Puerperium", *Brit. med. J.*, 1: 1245.

CALLENDER, S. T. (1944), "A Critical Review of Pernicious Anæmia of Pregnancy", *Quart. J. Med.*, 13: 75.

DAVIDSON, L. S. P. (1948), "Refractory Megaloblastic Anemia", *Blood*, 3: 107.

DAS GUPTA, C. R. (1954), "Anæmia in Pregnancy: A Critical Review. With Recommendations for Future Lines of Work in India", *Indian J. med. Res.*, 42: 411.

DAS GUPTA, C. R., CHATTERJEA, J. B., and BASU, P. (1953), "Vitamin B_{12} in Nutritional Macrocytic Anæmia", *Brit. med. J.*, 2: 645.

FAIRLEY, N. H., BROMFIELD, R. J., FOY, H., and KONDI, A. (1938), "Nutritional Macrocytic Anæmia in Macedonia: Preliminary Report", *Trans. roy. Soc. trop. Med. Hyg.*, 32: 132.

FORSHAW, J. W. B., THELWALL JONES, A., CHISHOLM, W. N., and MCGINLEY, W. K. (1957), "Megaloblastic Anæmia of Pregnancy and the Puerperium", *J. Obstet. Gynæc. Brit. Emp.*, 64: 255.

FOY, H., KONDI, A., and HARGREAVES, R. (1952), "Anæmias of Africans", *Trans. roy. Soc. trop. Med. Hyg.*, 46: 327.

GILES, C., and SHUTTLEWORTH, E. M. (1958), "Megaloblastic Anæmia of Pregnancy and the Puerperium", *Lancet*, 2: 1341.

KOTHARI, B. V., and BHENDE, M. (1949), "Nutritional Megaloblastic Anæmia: So-Called Pernicious Anæmia of Pregnancy. A Preliminary Report", *Indian J. med. Res.*, 37: 347.

KOTHARI, B. V., and BHENDE, M. (1952), "Nutritional Megaloblastic Anæmia of Pregnancy. A Study of 100 Cases", *Indian J. med. Res.*, 49: 387.

LAYRISSE, M., BLUMFELD, N., DUGARTE, I., and ROCHE, M. (1959), "Vitamin B_{12} and Folic Acid Metabolism in Hookworm-Infected Patients", *Blood*, 14: 1269.

LILLIE, E. W., GATENBY, P. B. B., and MOORE, H. C. (1954), "A Survey of Anæmia in 4,314 Cases of Pregnancy", *Irish J. med. Sci.*, page 304.

LUHBY, A. L. (1959), "Megaloblastic Anemia in Infancy", *J. Pediat.*, 54: 617.

MOORE, H. C., LILLIE, E. W., and GATENBY, P. B. B. (1955), "The Response of Megaloblastic Anæmia of Pregnancy to Vitamin B_{12}", *Irish J. med. Sci.*, page 106.

SCHOFIELD, F. D. (1957), "Aspects of Nutritional Anæmia in Pregnancy in Gambia", *Trans. roy. Soc. trop. Med. Hyg.*, 51: 221.

STRAUSS, M. B., and CASTLE, W. B. (1933), "Studies of Anemia in Pregnancy. 3. The Etiologic Relationship of Gastric Secretory Defects and Dietary Deficiency to the Hypochromic and Macrocytic (Pernicious) Anemias of Pregnancy and the Treatment of these Conditions", *Amer. J. med. Sci.*, 185: 539.

TASKER, P., RICHARDSON, A. M., and LLEWELLYN-JONES, D. (1956), "Anæmia in Pregnancy as Encountered in Malaya", *J. Obstet. Gynæc. Brit. Emp.*, 63: 409.

THOMPSON, R. B. (1957), "Seasonal Incidence of Megaloblastic Anæmia of Pregnancy and the Puerperium", *Lancet*, 1: 1171.

THOMPSON, R. B., and UNGLEY, C. C. (1951), "Megaloblastic Anæmia of Pregnancy and the Puerperium", *Quart. J. Med.*, 44: 187.

TUCK, I. M., and WHITTAKER, N. (1950), "Vitamin B_{12} in Idiopathic Steatorrhœa", *Lancet*, 1: 757.

Addendum.

Four of the women with megaloblastic anæmia from the Kerema area have been found to have excess hæmoglobin A2, and one of them has an associated abnormal hæmoglobin.

SPIRONOLACTONE USED WITH MERCAPTOMERIN IN THE TREATMENT OF CONGESTIVE CARDIAC FAILURE.

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THE 17-spirolactone-steroids are a group of compounds which antagonize the action of aldosterone and desoxycorticosterone on the renal tubule. The most potent drug of the series is spironolactone ("SC 9420") This drug, in combination with other diuretic agents, has been shown to be effective in treating œdema in many patients resistant to conventional therapy (Slater *et alii*, 1959; Bartter, 1960; Coppage and Liddle, 1960). In cases of cirrhosis of the liver with ascites, the use of spironolactone in combination with one of the benzothiadiazine diuretics (chlorothiazide and its derivatives) is a major therapeutic advance (Gantt and Dyniewicz, 1959; Sleisenger *et alii*, 1959; Clowdus *et alii*, 1960; North *et alii*, 1960; Shaldon *et alii*, 1960).

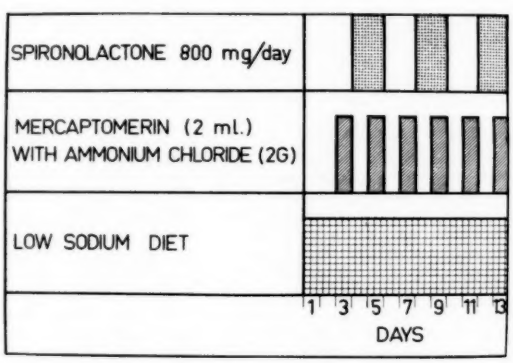

FIGURE I.
Details of the sequence of diuretic drugs used in the trial.

We have previously reported the use of spironolactone with hydrochlorothiazide in the treatment of resistant œdema (Farrelly *et alii*, 1960). In the earlier study, in all cases the addition of spironolactone caused a reduction in the high urinary potassium excretion, although the sodium diuresis achieved was relatively small. However, in one case combined therapy with spironolactone and hydrochlorothiazide caused a massive diuresis when hydrochlorothiazide alone had failed.

The purpose of the present investigation was to determine whether spironolactone improved the response of

TABLE I.
Clinical Details of Patients.

Case Number.	Patient's Age (Years) and Sex.	Diagnosis.	Œdema.			Treatment Month Prior to Trial.		
			Duration (Months).	Initial Degree.	Final Degree.	Bed-Rest.	Mersalyl.	Chlorothiazide.
I	57 : M.	Pulmonary heart disease.	6	Moderate.	Nil.	−	+	+
II	62 : M.	Rheumatic heart disease.	0·5	Moderate.	Nil.	−	−	−
III	46 : F.	Hypertensive heart disease.	3	Severe.	Nil.	−	+	+
IV	52 : M.	Cardiomyopathy.	6	Severe.	Nil.	−	+	+
V	65 : M.	Ischæmic heart disease.	1	Severe.	Mild.	−	−	+
VI	70 : M.	Ischæmic heart disease.	9	Moderate.	Nil.	−	−	+
VII	46 : M.	Ischæmic heart disease.	2	Severe.	Mild.	+	+	+

patients with severe congestive cardiac failure to mercurial diuretics.

Method.

The seven patients included in this study were admitted to a metabolic unit, kept at bed rest and maintained on a diet of constant sodium (22 mEq per day) and potassium (70 mEq per day) content, with a daily fluid intake limited to 1600 ml. A daily record was kept of the weight, blood pressure and volume of urine. Biochemical estimations included the daily urinary output of sodium, potassium and chloride, and serum sodium, potassium, chloride and bicarbonate, and blood urea levels were measured three times a week. The sodium and potassium contents were measured by the flame photometer, the chloride content by the method of Van Slyke and Hiller (1947).

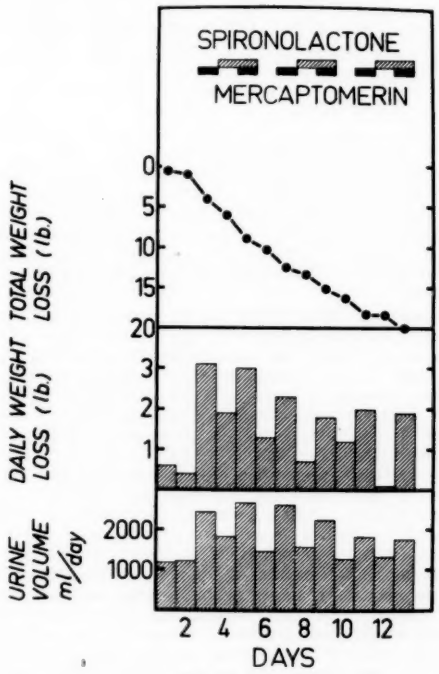

FIGURE II.
The mean changes in weight and urinary volume of the seven patients during the trial period.

The trial period of 13 days consisted initially of two days in bed on the sodium-poor diet, followed by six injections of mercaptomerin ("Thiomerin"), 2 ml. on alternate days; ammonium chloride (2 grammes) was given orally two hours before each dose of mercaptomerin. Spironolactone (800 mg. per day) was given orally in divided doses on the day before and the day of every alternate injection of mercaptomerin (see Figure I).

Results.

Clinical Aspects.

The seven patients studied were not suffering from œdema resistant to conventional therapy, although six had been given diuretics without a satisfactory response in the month before their admission to hospital (Table I). A diet of rigidly low sodium content had not previously been given to the patients, and only one patient had been on strict bed rest at home. Œdema, which had been present for two weeks to nine months, disappeared in five out of seven cases. The remaining two patients were left with some residual œdema, which in one patient was relieved by further therapy with spironolactone and mercaptomerin. The poor response of the other patient was associated with poor renal function; the blood urea level during the course of the trial rose from 39 to 65 mg. per 100 ml. (Case V).

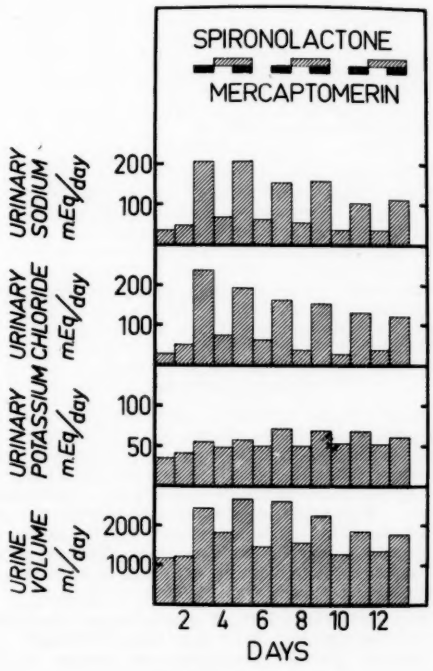

FIGURE III.
The mean values for the daily urinary volume and output of sodium, chloride and potassium of the seven patients in the trial.

All patients lost weight during the 13-day trial; the average loss of weight was 20 lb.; it varied in individual patients from 8 to 33 lb. (Figure II). On the day after each injection of mercaptomerin the loss of weight continued (Figure II). There was no increase in weight on

TABLE II.
Detailed Biochemical Data.

Urine: Sodium and Potassium Excretion and Volume (ml./day).	Case Number.	Day. 1	2	3 M[1] Given.	4 S[1] Given.	5 M and S Given.	6	7 M Given.	8 S Given.	9 M and S Given.	10	11 M Given.	12 S Given.	13 M and S Given.
Sodium (mEq per day)	1	83	93	237	70	222	159	277	136	224	35	94	34	112
	2	83	138	298	203	287	125	242	109	124	26	68	13	64
	3	9	9	568	148	368	61	250	42	230	63	172	64	208
	4	1	1	63	8	155	13	96	43	264	93	221	95	321
	5	48	46	79	30	116	51	36	30	103	21	50	49	32
	6	27	45	157	4	129	9	68	13	69	3	40	10	36
	7	4	3	6	15	186	6	100	4	96	12	61	2	11
	Mean	36	48	201	68	209	61	153	54	159	36	101	38	112
Potassium (mEq per day)	1	29	29	26	31	35	44	51	43	48	51	57	39	37
	2	49	72	67	102	93	105	83	82	87	90	106	72	103
	3	30	27	98	39	35	35	70	35	43	24	43	43	42
	4	25	22	74	55	80	60	101	71	85	75	96	89	93
	5	41	47	24	30	35	40	54	30	56	42	21	28	41
	6	51	61	68	58	77	49	68	54	80	53	76	56	68
	7	20	27	29	30	54	16	71	38	84	38	81	39	40
	Mean	35	41	55	49	58	50	71	50	69	53	69	52	61
Volume (ml. per day)	1	1760	1260	2310	1880	3260	2320	3270	2250	2490	1620	1620	1450	1780
	2	1380	2030	3135	3325	2910	1950	2600	1816	1920	1620	1520	1020	2020
	3	806	568	5120	1720	3120	1200	2650	870	2020	940	2045	1330	2040
	4	700	564	1960	1750	3300	1692	2870	2460	3580	2040	3320	1940	3670
	5	1400	1480	1216	1220	2040	1550	1030	1220	1644	970	690	1020	1240
	6	1700	1500	2350	1840	1960	1000	1780	1540	2100	1170	1920	1700	1630
	7	590	1070	1010	1030	2200	596	2010	860	1890	700	1760	920	1128
	Mean	1191	1210	2443	1823	2684	1472	2601	1574	2235	1294	1839	1340	1787

[1] M, mercaptomerin S, spironolactone.

this day, as has been reported by Gold (1960) when organic mercurial diuretics were given alone. On only two days out of 35 possible occasions did a patient gain weight on the day after a mercurial injection. There was a fall in the blood pressure of the four patients who lost the greatest amount of weight during the trial. One patient (Case III), who lost 33 lb. in weight, had a fall in blood pressure from 160/125 to 124/90 mm. of mercury. There were no side effects from the drugs during the trial period.

Urinary Excretion.

A summary of the results is given in Figure III, and the data are available in Table II. There is a wide individual variation in the response in any group of patients to a diuretic agent. One patient (Case VII) failed to respond to mercaptomerin until spironolactone was added. With this exception, mercaptomerin caused diuresis accompanied by an increased loss of sodium and chloride in all cases with each injection. The quantitative diuretic response to mercapotomerin was less in the same patient with each successive injection.

There was no serious loss of potassium in the urine of any patient, the greatest daily loss being 106 mEq. This was in contrast to hydrochlorothiazide, which caused a significant loss of potassium in all patients prior to the addition of spironolactone (Farrelly *et alii*, 1960).

There was a fall in the total urinary volume and urinary chloride excretion with successive injections of mercaptomerin. It was found that the sodium excretion on days 5, 9 and 13 (Figure I) during continued therapy was higher than would have been expected from the trends observed with chloride and urinary volume (Figure III). This could be interpreted as an effect of spironolactone in increasing the sodium diuresis. Spironolactone also altered the normal response to a mercurial diuretic on the day after injection (Gold, 1960).

Serum Electrolyte Levels.

There were no significant changes in the serum electrolyte levels during the trial, apart from the serum potassium level, which fell below the normal range in one patient. In Case V there was moderate impairment of renal function, and the blood urea level rose from 39 to 65 mg. per 100 ml. during the trial period.

Discussion.

There have been many reports of small groups of patients with œdema who have responded well to combined treatment with spironolactone and a benzothiadiazine diuretic (Bartter, 1960), but in only two series of cases has combined treatment with spironolactone and a mercurial diuretic been used (Page and Lavender, 1959; Gold, 1960).

Our study was undertaken to determine whether treatment with spironolactone in addition to a mercurial diuretic would cause a significant contribution to the diuresis and rate of recovery of the patient with severe congestive cardiac failure admitted to hospital because diuretic treatment at home had failed. With a single exception (Case VII), the patients under hospital conditions with bed rest and a preliminary two days on a sodium-poor diet responded to mercaptomerin. These cases could not therefore be regarded as examples of refractory œdema. Indeed, with congestive cardiac failure as opposed to ascites from liver disease, the number of genuine refractory cases when treatment is by bed rest, a sodium-poor diet and a mercurial or benzothiadiazine diuretic is relatively small, probably less than 1% (Rubin *et alii*, 1955). In most refractory cases there is an associated electrolyte disorder or renal impairment. In reports of cases of congestive cardiac failure, the term "refractory" has been used in a relative rather than an absolute sense. There are as yet no accepted criteria of what constitutes a "refractory" case.

In the present study, on the days of the mercurial injection the effect of spironolactone was of no clinical significance, although it did cause a slight increase in the sodium diuresis. Gold (1960), using a mercurial diuretic alone, showed convincingly that in the first 24 hours after the injection there was a considerable loss of weight, but that during the next 24 hours there was a corresponding gain in weight which might vary from 1 to 2 lb. This compensatory gain was reported to occur in almost all patients with œdema treated in this manner. Observations in our hospital have confirmed that a compensatory weight gain does occur in most patients on the day after the injection of a mercurial diuretic (Otway, 1960). Gold (1960) called this response the "antidiuretic 'alarm' reaction", assuming that it was mediated through the adrenal glands. In one case he reported that spironolactone given with the mercurial diuretic prevented this

reaction from occurring, and that the diuresis and loss of weight which occurred in the first 24 hours continued to a lesser extent into the next. In the seven cases in our series this was a striking finding. There were only two occasions out of 35 possible days when the weight of the patient increased in the second 24 hours after an injection of mercaptomerin (see Figure II).

Page and Lavender (1959), in two cases of resistant congestive cardiac failure, observed that spironolactone augmented the diuretic effect of hydrochlorothiazide, but not the action of mercaptomerin.

In normal people, in patients with cirrhosis of the liver and ascites, and from results observed in cases of primary aldosteronism, it is apparent that spironolactone influenced the urinary sodium-potassium ratio on the day after treatment was stopped. By the second day after the cessation of therapy, the ratio on varied sodium intake had returned to a pre-treatment level (Bartter, 1960; Liddle, 1960; Biglieri, 1960). Spironolactone, therefore, in the present trial, affected significantly only every second injection of mercaptomerin.

In contrast to observations on the acute effects of spironolactone, there have been claims (Clowdus *et alii*, 1960) that in cirrhosis of the liver spironolactone may take one to two weeks to produce a maximum diuresis. This observation is difficult to explain on present knowledge of the mode of action of spironolactone (Bartter, 1960).

A fall in blood pressure with spironolactone has previously been reported in hypertensive patients (Hollander *et alii*, 1960). In the one case in the present study in which hypertension was the cause of the heart failure, there was a striking fall in blood pressure; this patient also lost the greatest amount of œdema fluid. Although Hollander *et alii* (1960) concluded that changes in the fluid balance in the various compartments of the body might play a part in the fall of blood pressure, yet in their paper there was evidence that this was not the only mechanism involved.

From our study it is concluded that spironolactone prevents the fluid retention usually observed on the day after a mercurial injection, but the effect in augmenting the diuretic action of mercaptomerin on the day of injection is slight. The overall effect of giving spironolactone to these patients has been to shorten to some extent the time required to remove the œdema fluid. Spironolactone is costly and should be reserved for use in the treatment of patients who have proved refractory to conventional therapy with the more potent benzothiadiazine and mercurial diuretics.

Summary.

Spironolactone, which is an aldosterone antagonist, was used in conjunction with the organic mercurial diuretic mercaptomerin in seven cases of congestive cardiac failure. Although it influenced the pattern of the diuretic response, particularly on the day after the mercurial injection, yet the effect of combined therapy was not sufficiently striking to justify the use of spironolactone except in cases that had proved refractory to conventional diuretics, of which there was one in the present series.

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References.

BARTTER, F. C. (1960), "The Clinical Use of Aldosterone Antagonists", Thomas, Springfield.

BIGLIERI, E. G. (1960), "The Clinical Use of Aldosterone Antagonists", Thomas, Springfield.

CLOWDUS, B. F., HIGGINS, J. A., ROSEVEAR, J. W., and SUMMERSKILL, W. H. J. (1960), "Treatment of 'Refractory' Ascites with a New Aldosterone Antagonist in Patients with Cirrhosis", *Proc. Mayo Clin.*, 35: 97.

COPPAGE, W. S., and LIDDLE, G .W. (1960), "Mode of Action and Clinical Usefulness of Aldosterone Antagonists", *Curr. ther. Res.*, 2: 239.

FARRELLY, R. O., HOWIE, R. N., and NORTH, J. D. K. (1960), "Use of Spironolactone and Hydrochlorothiazide in Treatment of Œdema", *Brit. med. J.*, 2: 339.

GANTT, C. L., and DYNIEWICZ, J. M. (1959), "Some Effects of 17-spirolactosteroids on the Edema of Cirrhosis, with Observations on a New Spirolactone Derivative", *Clin. Res.*, 7: 294.

GOLD, H. (1960), "The Clinical Use of Aldosterone Antagonists", Thomas, Springfield.

HOLLANDER, W., CHOBANIAN, A. V., and WILLIAMS, R. W. (1960), "The Clinical Use of Aldosterone Antagonists", Thomas, Springfield.

LIDDLE, G. W. (1960), "The Clinical Use of Aldosterone Antagonists", Thomas, Springfield.

NORTH, J. D. K., HOWIE, R. N., and FARRELLY, R. O. (1960), unpublished data.

OTWAY, W. F. (1960), personal communication.

PAGE, R. G., and LAVENDER, A. R. (1959), "The Effect of 3-(3-Oxo-7 Alpha-Acetylthio-17 Beta-Hydroxy-4-Androsten-17 Alpha-YL)-Propionic Acid Lactone (SC.9420) on Edematous Cardiac Patients", *J. Lab. clin. Med.*, 54: 933.

RUBIN, A. L., THOMPSON, H. G., BRAVEMAN, W. S., and LUCKEY, E. H. (1955), "The Management of Refractory Edema in Heart Failure", *Ann. intern. Med.*, 42: 358.

SHALDON, S., MCCLAREN, J. R., and SHERLOCK, S. (1960), "Resistant Ascites Treated by Combined Diuretic Therapy", *Lancet*, 1: 609.

SLATER, J. D. H., MOXHAM, A., HURTER, R., and NABARRO, J. D. N. (1959), "Clinical and Metabolic Effects of Aldosterone Antagonists", *Lancet*, 2: 931,

SLEISENGER, M. H., RICHARD, J., KOWLESSAR, O. D., CLARKSON, B., THOMPSON, D., and PETERSON, R. E. (1959), "Effects of Spirolactones on Excretion of Water and Electrolytes, and on Aldosterone Metabolism in Cirrhosis", *J. clin. Invest.*, 38: 1043.

VAN SLYKE, D. D., and HILLER, A. (1947), "Application of Sendroy's Iodometric Chloride Titration to Protein-Containing Fluids", *J. biol. Chem.*, 167: 107.

A REVIEW OF 20 CASES OF APLASTIC ANÆMIA.

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PANCYTOPENIA associated with bone marrow aplasia was first described by Ehrlich (1888). He found severe anæmia and a low white-cell count with a relative lymphocytosis, and predicted that the red marrow would be found to be fatty. This proved so at autopsy. Since then many terms have been used to describe conditions where part or all of the circulating blood cells are deficient irrespective of the cellularity of the bone marrow.

Because of varying appearances of the aspirated marrow in otherwise clinically similar cases, Bomford and Rhoads (1941) preferred the term "Refractory Anæmia". However, they included anæmias secondary to specific chronic diseases and some with a megaloblastic marrow which did not respond to conventional treatment.

Schultz (1922) showed that the granulocytes only could be decreased in number, and Kracke (1931) associated agranulocytosis with amidopyrine and other drugs made from coal-tar derivatives. As the number of drugs and chemicals for use in home and factory has increased, so have reports of blood disorders associated with their medication or contact, and it has become clear that agranulocytosis, thrombocytopenia and hypoplasia of erythropoiesis may occur separately or together.

Mohler and Leavell (1958) reviewed 302 cases of aplastic anæmia from various series, including 50 cases of their own collected between 1933 and 1956. They considered that only 21% of the 302 patients gave a positive history of toxic exposure. De Gruchy (1958) on the other hand states that the commonest cause of aplastic anæmia is a drug or chemical, and he considers it possible that in many cases of so-called primary aplastic anæmia the toxic agent has not been identified.

The fact that the marrow aspirate is sometimes hypercellular may cause difficulty in diagnosis. Boon and Walton (1951), in their series of 25 cases, found hypercellular marrow in five on aspiration. There was no correlation between the marrow findings and the course or severity of the disease. As de Gruchy (1958) points out, the marrow may vary from aplasia to hyperplasia from different sites in the same patient.

Some drugs, such as busulphan, 6-mercaptopurine and nitrogen mustard, regularly cause marrow depression. Other drugs may cause blood dyscrasias in an apparent random manner.

In this paper are presented 20 cases of marrow aplasia followed in the department of hæmatology, Royal Perth Hospital, Western Australia, over the last four years. All except one of the living patients have been observed for more than one year. No cases of chronic disease normally involving the bone marrow were included. Cases in which marrow depression occurred while the patient was on a known regular marrow depressant (for example, 6-mercaptopurine) were excluded.

TABLE I.

Some Clinical Details of Cases in the Series.

Case Number.	Sex.	Age. (Yrs.)	Outcome.	Incriminated Drug or Chemical.	Peripheral Blood Picture.
I	M.	27	Alive.	Lindane or D.D.T.	Pancytopenia.
II	M.	31	Alive.	Lindane or D.D.T.	Pancytopenia.
III	M.	33	Deceased.	Sulphatriad.	Pancytopenia.
IV	F.	36	Alive.	? "Achromycin", ACTH.	Pancytopenia.
V	F.	36	Deceased.	Chloramphenicol.	Pancytopenia.
VI	F.	40	Deceased.	"Salazopyrin" and gold.	Pancytopenia.
VII	F.	48	Deceased.	Gold and phenylbutazone.	Pancytopenia.
VIII	F.	54	Deceased.	Gold.	Pancytopenia.
IX	F.	60	Deceased.	"Dindevin", antituberculosis drugs.	Pancytopenia.
X	F.	63	Alive.	Phenylbutazone.	Pancytopenia.
XI	M.	64	Alive.	"Dilantin."	Pancytopenia.
XII	F.	67	Deceased.	"Apresoline", "Serpasil".	Pancytopenia.
XIII	F.	70	Alive.	Phthalylsulphathiazole.	Pancytopenia.
XIV	M.	74	Alive.	Gold.	Pancytopenia.
XV	F.	75	Alive.	None known.	Pancytopenia.
XVI	F.	49	Deceased.	Methylthiouracil.	Agranulocytosis.
XVII	M.	71	Deceased.	Sulphapyridine.	Agranulocytosis.
XVIII	M.	77	Deceased.	"Sulphatriad."	Agranulocytosis.
XIX	M.	82	Deceased.	None known.	Agranulocytosis.
XX	F.	70	Alive.	Gold.	Thrombocytopenia.

Analysis of 20 Cases.

Twelve of the 20 patients were female and eight were male. Five females and four males are surviving. The age of onset ranged from 27 to 82 years and 11 patients were aged 60 years or more. All the patients were of European descent. Six of the 20 were of Italian or Greek extraction and the rest were of Northern European origin.

Fifteen patients had a convincing history of taking a drug capable of producing marrow aplasia prior to developing their symptoms. Two were exposed to lindane (benzene hexachloride) and DDT. In the other three cases no definite exposure could be found, although one patient had received "Achromycin" and ACTH just prior to the onset of her aplasia.

Fifteen patients showed depression of all three cellular blood elements. Four patients had granulocytopenia only, and one patient showed thrombocytopenia alone.

Clinical Findings.

Table I shows some of the relevant findings in these patients. Patients I to XV suffered from pancytopenia, patients XVI to XIX from agranulocytosis and patient XX from thrombocytopenia.

Most of the patients with pancytopenia presented with tiredness of slow onset and spontaneous bruising or hæmorrhage. The seven patients that died did so with signs of hæmorrhage from multiple sites with or without added infection.

The four patients with agranulocytosis all presented with high fever and signs of an overwhelming infection. Their illnesses, all of sudden onset, ran short, stormy courses of a few days and they all died, despite intensive chemotherapy and immediate cessation of the suspected offending drug.

Bone Marrow Findings.

Ten of the 15 patients with pancytopenia showed aplasia of all three elements. In four erythropoiesis was, either normal or increased with depression of the other two elements, but subsequent marrow examination revealed total aplasia. One patient had normal erythroid and myeloid cellularity with absence of megakaryocytes. The aspiration was not repeated. The marrow findings in the four patients with agranulocytosis showed depression of granulopoiesis alone. Patient XX, presenting with thrombocytopenia, showed an absence of megakaryocytes in the marrow aspirate.

Relation of Aplasia to Drugs and Other Chemicals.

As mentioned earlier, in 15 cases there was reliable evidence of drug-induced aplasia. Further details concerning the incriminated drug or chemical and the condition for which it was used are given in Table II.

In 13 of the 15 patients with pancytopenia there was a history of drug administration or contact with chemicals known to cause marrow depression. In 10 of these the drug or chemical had been discontinued some weeks prior to the onset of symptoms. The drugs involved in more than one case were gold salts, phenylbutazone and sulphonamides.

Two patients had not been taking drugs, but both had used extensively a spray of DDT and lindane (benzene hexachloride) about one month prior to the onset of symptoms.

Three patients with agranulocytosis had all been taking drugs up to the time of the onset of symptoms. One of these had been treated with methylthiouracil six years before with no untoward effect and had been replaced on the drug two weeks before her final admission to hospital. In the other two cases, sulphonamide was the drug incriminated. The patient with thrombocytopenia had had gold injections for rheumatoid arthritis.

One patient with pancytopenia and one with agranulocytosis had no history of exposure to drug or chemical. Patient IV had been given "Achromycin" (tetracycline hydrochloride) and ACTH, but these are not considered likely causes of the bone marrow depression.

Treatment.

The patients were treated by conventional methods. The incriminating drug or chemical was removed when it was known. The patients were transfused till their hæmoglobin levels were compatible with their activity. Infections as they arose were treated with antibiotics. Corticosteroids were administered if a bleeding tendency existed. One patient with aplasia due to gold received treatment with British anti-Lewisite (dimercaprol) with no beneficial effect. The patient with thrombocytopenia was subjected to splenectomy, with no improvement in the platelet count.

Reports of Cases.

Pancytopenia.

CASE I.—An Italian bricklayer, aged 27 years, was admitted to hospital on February 7, 1957, with a history of easy bruising and intermittent bleeding of the gums for one month. For two weeks before his admission he had been feeling tired. He developed tonsillitis three days before admission. On examination he was seen to have multiple petechial spots over the skin and on the palate. His gums were bleeding spontaneously. The tonsils were grossly enlarged and contained abundant exudate; the draining cervical lymph glands were enlarged and tender. The spleen was not palpable. The Hess test gave a positive result. The

TABLE II.
Further Clinical Details of Cases in the Series.

Case Number.	Condition for Which Drug was Given.	Incriminated Drug or Chemical.	Amount or Duration of Medication.	Time Interval Between Cessation of Drug Therapy and Onset of Symptoms.
I	Nil.	D.D.T., lindane (benzene hexachloride).	?	4 weeks.
II	Nil.	D.D.T., lindane.	?	4 to 8 weeks.
III	Pneumonia.	"Sulphatriad."	25 grammes.	6 to 8 weeks.
IV	Asthma.	"Achromycin" (tetracycline hydrochloride), ACTH.	?	4 weeks.
V	Infected nipple.	Chloramphenicol.	15 grammes.	8 weeks.
VI	Ulcerative colitis.	"Salazopyrin" (salicylazosulphapyridine).	6 grammes.	2 weeks.
		Succinylsulphathiazole.	120 grammes.	8 weeks.
		Gold.	5 injections.	6 weeks.
VII	Rheumatoid arthritis.	Gold.	5 injections.	4 weeks.
		Phenylbutazone.	200 mg. per day for 6 months.	
VIII	Rheumatoid arthritis.	Gold.	6 injections.	4 weeks.
IX	Pulmonary tuberculosis.	Streptomycin, isoniazid and paraaminosalicyclic acid.	5 months.	None.
	Thrombophlebitis.	"Dindevan."	10 days.	8 weeks.
X	Osteoarthritis.	Phenylbutazone.	2 years.	8 weeks.
XI	Epilepsy.	"Dilantin" (phenytoin sodium).	4 years.	None.
XII	Hypertension.	Hydralazine. "Serpasil" (reserpine).	6 years.	None.
XIII	Diverticulitis.	Phthalylsulphathiazole.	1 week.	4 weeks.
XIV	Arthritis.	Gold.	2 courses.	? 6 months.
XV	Nil.	None known.	Nil.	—
XVI	Thyrotoxicosis.	Methylthiouracil.	1954 and two weeks before death.	None.
XVII	Dermatitis herpetiformis.	Sulphapyridine.	2 months.	None.
XVIII	Diarrhœa.	"Sulphatriad."	15 grammes.	1 day.
XIX	Nil.	None known.	Nil.	—
XX	Rheumatoid arthritis.	Gold.	1 course	? 12 weeks.

hæmoglobin level was 9·2 grammes per 100 ml. and the packed-cell volume was 27% as estimated by the Wintrobe method. A white-cell count yielded a total figure of 2400 per cubic millimetre, with 24% neutrophils, 66% lymphocytes, 8% monocytes and 2% eosinophils and 11,000 platelets per cubic millimetre. Two attempts at marrow aspiration were made. The first, from the manubrium sterni, was unsatisfactory. The second, from the body of the sternum, showed a fair number of small fragments which were hypocellular. Both erythropoiesis and granulopoiesis were reduced. No megakaryocytes were seen. The ratio of lymphocytes to other marrow constituents was increased. A diagnosis of marrow aplasia was made. On June 5, 1957, a bone marrow biopsy from the right ileum was performed. The marrow cavity contained mostly fatty tissue with a few remnants of the original marrow. There was no history of drug taking. During December, 1956, the patient had been assisting a relative to "dip" sheep, but the exact nature of the sheep-dip is not known. His house was without fly-wire and during the summer months (November to February) he himself had sprayed his house several times per day with a mixture of D.D.T. and lindane. The patient was transfused till his hæmoglobin level reached 11·8 grammes per 100 ml. His tonsillitis settled spontaneously and the Hess test gave a negative result. He was discharged from hospital on a regime of 10 mg. of prednisolone twice daily. Subsequently he was transfused when necessary and in September, 1957, testosterone propionate (100 mg. three times per week) was added to the therapy for a period of three months. His transfusion requirements slowly decreased during 1958; the prednisolone dosage was reduced to 5 mg. twice daily and was finally ceased in February, 1959. He has remained well since February, 1959, requiring no transfusions, and a blood count done on November 30, 1959, showed a hæmoglobin level of 15·0 grammes per 100 ml., a packed-cell volume (Wintrobe) of 43%, 6100 leucocytes per cubic millimetre, with 50% neutrophils, 41% lymphocytes, 8% monocytes and 1% eosinophils and 77,000 platelets per cubic millimetre. No further marrow biopsy was done. The patient was warned of the dangers of reexposure to sheep-dip and insecticides.

CASE V.—A housewife, aged 36 years, was admitted to hospital on May 20, 1959, with bruising. Eight weeks before her admission she had had a course of chloramphenicol therapy for a discharging nipple. Six weeks before her admission she was treated at home for jaundice with pale stools and some vague abdominal pain. Four weeks before admission bruising began, mostly on the legs, but also on the arms and face. She had menorrhagia on admission. On examination she had extensive purpura and the Hess test gave a positive result. The spleen was not palpable. The hæmoglobin level was 5·5 grammes per 100 ml.; there were 3300 leucocytes per cubic millimetre, with 14% neutrophils, 83% lymphocytes, 2% monocytes and 1% eosinophils and the platelets totalled 8000 per cubic millimetre. Marrow was aspirated easily from the manubrium sterni. Fragments and trails were hypocellular. Erythropoietic and myelopoietic cells were very infrequent and megakaryocytes were not seen. The patient was transfused and the menorrhagia decreased. She was treated with prednisone (20 mg. six-hourly). However, eight days after her admission to hospital she developed hæmaturia and shortly afterwards showed signs of a right-sided cerebral hæmorrhage, from which she died. No autopsy was performed.

Agranulocytosis.

CASE XVII.—This male, aged 70 years, died soon after his admission to hospital on July 24, 1957. In February, 1957, he developed a rash on his limbs which was diagnosed as erythema multiforme and later as pemphigus. At that time he was given local treatment with ichthyol cream and systemic cortisone and "Achromycin". The lesions recurred in May and a biopsy then showed the diagnosis to be dermatitis herpetiformis. The cortisone was slowly stopped and he received sulphapyridine (0·5 gramme thrice daily) from then until his death. On the day of admission he suddenly developed a high fever and became delirious. Three blood examinations in February, April and June showed a polymorph leucocytosis. The count on the last admission was 740 leucocytes per cubic millimetre, all of which were lymphocytes. Bone marrow aspiration showed normal erythropoiesis and numerous megakaryocytes, but no cells of the granulocytic series.

Discussion.

These patients with bone marrow depression have not presented any previously unreported features. Nine of a total of 20 still survive; however, only five have been discharged from out-patient care and are leading normal lives. The remainder are still under observation and require some type of therapy. Treatment is often prolonged and necessitates many hospital admissions for blood transfusions.

Six of the patients were of Italian or Greek origin. There is probably no significance in this finding, since there has been a considerable influx of migrants into Western Australia. Other authors have not reported any particular racial incidence except Mohler and Leavell (1958), who found only six Negroes in a total of 196 patients.

A probable ætiological agent was found in 17 cases, a higher percentage than that indicated by other authors. All the probable agents have been listed previously as occasional bone marrow depressants. Gold salts, phenylbutazone and sulphonamides were responsible for half the cases and these drugs are well known for this complication. Chloramphenicol was incriminated in one case only. The low incidence probably reflects more cautious use of the drug since marrow aplasia was first reported

(Rich *et alii*, 1950). Chloramphenicol aplasia has been reported in Britain (Hodgkinson, 1954) and in Australia (Shaw and McLean, 1957). The patient in this series developed jaundice at the onset of her illness and this association has been noted by others. Benzene hexachloride (lindane) and DDT have been incriminated previously in aplastic anæmia (Clinico-Pathological Conference, 1955; Current Comment, 1956).

Osgood (1953) pointed out that there is often a time interval between the cessation of drug therapy and the appearance of symptoms of aplastic anæmia, and this was seen in 12 of the 15 cases of pancytopenia reported here.

In contrast to the above, the three patients with agranulocytosis caused by drugs were receiving therapy up to the time of admission to hospital. Symptoms occurred suddenly and it is doubtful if routine blood examinations would have prevented this complication. The patient reported in detail as Case XVII had several white-cell counts performed routinely while receiving sulphapyridine. These showed a polymorph leucocytosis until the final illness. All four patients with agranulocytosis died from overwhelming infection after a very short illness and in spite of antibiotic therapy.

Summary.

Twenty cases of bone marrow depression are reviewed. Four patients presented with agranulocytosis, one with thrombocytopenia and the remainder with pancytopenia. In 17 cases a suspected ætiological agent was discovered. Gold salts, phenylbutazone and sulphonamides accounted for half the cases.

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References.

BOMFORD, R. R., and RHOADS, C. P. (1941), "Refractory Anæmia", *Quart. J. Med.*, 10: 75.

BOON, T. H., and WALTON, J. H. (1951), "Aplastic Anæmia", *Quart. J. Med.*, 20: 75.

CLINICOPATHLOGICAL CONFERENCE (1955), "Exposure to Insecticides and Bone Marrow Failure", *Amer. J. Med.*, 19: 274.

CURRENT COMMENT (1956), "Aplastic Anæmia and Insecticide Vaporizers", MED. J. AUST., 1: 618.

DE GRUCHY, G. C. (1958), "Clinical Hæmatology in Medical Practice", Blackwell, Oxford.

EHRLICH, P. (1888), *Charité Ann.*, 13: 300.

HODGKINSON, R. (1954), "Blood Dyscrasias Associated with Chloramphenicol. An Investigation into Cases in the British Isles", *Lancet*, 1: 285.

KRACKE, R. R. (1938), "Relation of Drug Therapy to Neutropenic States", *J. Amer. med. Ass.*, 111: 1255.

MOHLER, D. N., and LEAVELL, B. J. (1958), "Aplastic Anæmia. An Analysis of 50 Cases", *Ann. intern. Med.*, 49: 326.

OSGOOD, E. E. (1953), "Drug Induced Hypoplastic Anæmia and Related Syndromes", *Ann. intern. Med.*, 39: 1173.

RICH, M. L., RITTERHOFF, R. J., and HOFFMANN, R. J. (1950), "A Fatal Case of Aplastic Anæmia following Chloramphenicol Therapy", *Ann. intern. Med.*, 33: 1459.

SCHULTZ, W. (1922), *Dtsch. med. Wschr.*, 48: 1495.

SHAW, R. G., and MCLEAN, J. A. (1957), "Chloramphenicol and Aplastic Anæmia", MED. J. AUST., 1: 352.

PEMPIDINE IN THE TREATMENT OF HYPERTENSION.

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PEMPIDINE, an orally effective hypotensive agent with a ganglion-blocking action, has been used at the Cardio-Vascular Clinic, Sydney Hospital, since August, 1958. We have now treated 13 patients for periods up to 24 months, and are here reporting our experience with this drug in the treatment of hypertensive disease, up to August, 1960.

Pharmacology.

Pempidine (1=2=2=6=6 pentamethylpiperidine), a tertiary amine, is the first piperidine derivative with ganglion-blocking activity to be used therapeutically in humans. The pharmacological properties of this drug were investigated independently and contemporaneously by Spinks and Young (1958), and by Harington *et alii* (1958). Like mecamylamine, pempidine is virtually completely absorbed from the intestine, appears to have a similar mode of action within the sympathetic and parasympathetic ganglia, and is more slowly excreted in an alkaline urine, although this latter effect is not so pronounced as in the case of mecamylamine.

After a single oral dose of pempidine, a hypotensive effect is usually observed within an hour, the maximal effect lasts one to three hours, and the total duration of hypotensive action is six to eight hours. Its effect is prolonged when its excretion is delayed in the presence of renal impairment.

In contrast to mecamylamine, pempidine is not significantly bound to plasma protein, and most of the recoverable drug from a single dose is passed in the urine within seven hours after ingestion. A further point of contrast related to its short action and rapid excretion is that the dosage of pempidine may be altered daily, if necessary, provided of course that renal function is satisfactory.

Subjects.

From August, 1958, to August, 1960, 13 patients have been treated for 24 months with pempidine at the Cardio-Vascular Clinic, Sydney Hospital. There were 12 females and one male, with ages ranging from 29 to 58 years. The criteria for treatment were those outlined in previous publications (Bauer, 1955; Bauer *et alii*, 1957), and accordingly, only patients with severe hypertension were treated. Some details and response to treatment of these patients are shown in Table I. Eight of the patients were believed to have renal disease with hypertension, and five essential hypertension. Two patients had obvious renal insufficiency (blood urea nitrogen level greater than 25 mg. per 100 ml. at the beginning of treatment). Four patients showed no electrocardiographic evidence of left ventricular hypertrophy, while four showed the changes of left heart strain. None had frank papilloedema.

Technique of Treatment.

All patients were thoroughly investigated as to the cause of their hypertension, along lines previously published. All patients were warned of the parasympathetic side effects and the effects of hypotension, and were advised how to combat them. All patients were encouraged to be ambulant during treatment, and, whether treatment was commenced in the ward or the out-patient clinic, blood pressures were taken at hourly intervals during the day, to determine the individual response to treatment, and until a satisfactory dosage schedule was reached.

Treatment was usually started with a dosage of 2·5 mg. given four times daily at intervals of five hours. When there was any degree of renal impairment, only 1 mg. was used for initial therapy once or more than once daily according to the effect on blood pressure. The dosage was altered daily as necessary, this being considered a safe procedure. Generally, little difficulty was found in reaching a satisfactory dosage of this drug for each individual in a short time.

Results.

Blood-Pressure Control.

The blood-pressure response was satisfactory and in most cases, the systolic pressures being normally reduced more than the diastolic. The postural effect was similar

TABLE I.

Case Number.	Patient's Sex and Age (Years).	Fundus Oculi Changes (Grade).	Electro-cardio-graphic Changes (Grade).	Blood Urea Nitrogen Level (mg. per 100 ml.).	Blood Pressure Before Treatment (mm. of Mercury).	Treatment.		Blood Pressure During Treatment (mm. of Mercury).	Severity of Symptoms.				Success or Failure.	Comments.
						Daily Dose (mg.).	Duration (Mths.).		Hypotensive.	Visual.	Bowel.	Mouth.		
I	F. : 29	III	0	9	240/140	10	6	120/100	0	1	2	1	F.	Constipation ++.
II	F. : 42	I	I	9	230/130	15	21	135/105	0	0	1	1	S.	
III	M. : 58	II	III	22	240/140	15	19	220/120	0	0	2	0	F.	Constipation ++.
IV	F. : 44	III	II	17	290/170	7·5	24	160/110	0	1	2	1	S.	
V	F. : 50	II	III	11	200/150	24	22	130/95	1	1	1	0	S.	
VI	F. : 29	I	0	9	230/160	30	18	150/110	0	1	2	1	S.	Pempidine only.
VII	F. : 37	II	III	13	210/140	10	13	130/100	0	1	0	0	S	Vitreous hæmorrhage left eye.
VIII	F. : 32	III	I	23	260/170	25	14	130/90	0	1	1	1	S.	
IX	F. : 36	II	0	21	240/160	120	18	220/110	0	0	0	1	S.	Chlorothiazide only recently added.
X	F. : 42	0	0	9	240/145	15	17	170/110	0	0	1	1	S.	
XI	F. : 48	I	II	12	230/140	30	18	150/100	0	1	2	0	F.	Constipation ++.
XII	F. : 44	III	III	42	205/140	5	8	180/130	0	1	1	1	S	Died; uræmia.
XIII	F. : 27	III	I	90	250/140	7·5	3	170/115	1	1	1	1	S.	Died; uræmia.

to that of mecamylamine, being quite definite, and the patients were encouraged to sleep propped up, and, when indicated, the bedtime dosage of pempidine was increased. Pempidine was given three to four times daily according to the individual's response to treatment and the duration of an adequate hypotensive effect. Sometimes the effective duration was as short as one hour.

Treatment was regarded as being successful in eight of the 13 cases, the blood pressure being satisfactorily controlled without undue complaint of side effect. In two further cases (XII and XIII), we were satisfied with the reduction of blood pressure from severe to moderately severe levels, because further reduction was associated with increased blood urea nitrogen levels. These were the two patients with obvious renal insufficiency prior to treatment, and in so far as no further reduction in blood pressure was desirable, treatment was regarded as being successful.

The daily maintenance dose of pempidine ranged from 5 to 120 mg., but was generally between 10 and 30 mg. All three unsuccessfully treated patients were excessively troubled by constipation, for which reason mecamylamine treatment had previously been abandoned.

Hypotensive Crises.

Symptoms attributable to hypotension were troublesome in only two of the patients treated. In one, the symptom was controlled by the addition of reserpine, which permitted the reduction of pempidine dosage; the other patient was suffering from gross renal insufficiency, and required close supervision.

Side Effects.

As with mecamylamine (Bauer *et alii*, 1959), the major side effect was constipation, and in some instances this was sufficiently distressing to prevent continuation of therapy. Visual difficulty and dryness of the mouth occurred with equal incidence, but were never disabling.

The true incidence of side effect with this drug likely to prevent continued therapy is not represented here, because all except three of the patients treated were given chlorothiazide or "Serpasil" or both at the beginning of treatment, or shortly after. It was soon found that, as with mecamylamine, the dosage of pempidine could be reduced by as much as 50% in some cases by the addition of these drugs. In no case was there any instance of undesirable effect on the central nervous system, as can occur with mecamylamine.

Discussion.

Our experience with pempidine, although by no means extensive, has been reported because so little has been written on the subject. The number of patients treated is sufficient to show that the drug can be successfully used, and that the response to treatment compares favourably with that of mecamylamine.

The advantage of this drug is its short duration of action, and this probably accounts for the infrequent complaint of symptoms due to excessive hypotension. Completeness of excretion during the night often allows the bowels to open before the day's dosage begins, or, if necessary, the morning dose can be delayed. This is a distinct advantage over mecamylamine, whose action is prolonged. In those patients with renal insufficiency, the risk of prolonged hypotension from excessive dosage is believed to be less with pempidine than with other ganglion-blocking drugs.

The disadvantage of pempidine is that it usually has to be taken four times daily, and there is probably loss of control of blood pressure at some stage during the night, except, of course, in those patients whose renal function is greatly impaired.

Mecamylamine has been our first choice for the control of hypertension, often together with chlorothiazide or reserpine or both; but from time to time, patients with troublesome side effects or renal insufficiency have been more safely controlled with pempidine.

With reference to the newer and more selective ganglion-blocking agent, bretylium tosylate, and guanethidine, our experience wiht the former, while encouraging, has not been entirely satisfactory, and will be the subject of a further paper from this clinic; and the latter, while so far giving highly satisfactory results, has not been used for a sufficiently long period in this clinic for a true assessment of its worth to be made.

Summary.

The results of treatment of 13 severely hypertensive patients with the ganglion-blocking agent pempidine for periods up to 24 months are described. Ten of the 13 patients were successfully treated, and included in the successes are two cases in which rising blood urea nitrogen levels prevented further reduction of blood pressure. The commonest side effect was constipation. Results as satisfactory as those with mecamylamine can be reproduced, and for reasons given, pempidine is a safer drug in selected cases.

Acknowledgements.

May and Baker (Australia) Pty. Ltd. made available adequate supplies of "Perolysen" and otherwise assisted in all possible ways. The nursing and medical staff of the Cardio-Vascular Clinic and of the Clinical Research Ward have together conducted the "clinical trial" of this drug, and have been of great assistance with the collection of information and, when necessary, offered helpful criticism.

References.

BAUER, G. E. (1955), "Practical Management of Severe Hypertension with Ganglion Blocking Agents", MED. J. AUST., 2: 727.

BAUER, G. E., EDWARDS, A. W. T., RITCHIE, F. L., and WHYTE, H. M. (1959), "Mecamylamine in the Treatment of Hypertension", MED. J. AUST., 2: 33.

BAUER, G. E., RITCHIE, F. L., and WHYTE, H. M. (1957), "'Ecolid' in the Treatment of Hypertension", MED. J. AUST., 2: 427.

SPINKS, A., and YOUNG, E. H. P. (1958), "Polyalkylpiperidines: A New Series of Ganglion-Blocking Agents", *Nature*, 181: 1397.

Reports of Cases.

MENINGOCOCCAL MENINGITIS: AN UNUSUAL ONSET.

By CAPTAIN P. JAMES, B.M., B.Ch. (Oxford),
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Clinical Record.

THE patient was an army recruit, aged 21 years, and was first seen complaining of severe abdominal colic of eight hours' duration, which radiated from his left lumbar region to the front of his left thigh. He had vomited several times, and urination had been painful after the commencement of the colic. He gave no relevant previous medical history. He looked pale and anxious, and was rolling about during crises of pain at 5 to 10-minute intervals. His pulse rate was 100 per minute, his blood pressure was 130/90 mm. of mercury and his temperature was 103° F. He was tender on the left side of his abdomen and also on percussion over his left costo-vertebral angle, but no other abnormalities were found; in particular his neck was not stiff, Kernig's sign was absent and he had no purpura. These signs were specifically sought because of the local prevalence of meningococcal infection. Microscopic examination of the urine showed only a few amorphous crystals, and plain X-ray films of the urinary tracts were normal.

The initial diagnosis was left ureteric calculus obstruction, with associated renal infection causing the pyrexia. The patient was admitted to hospital and treated with penicillin, chloramphenicol and analgesics. Eight hours after admission he began to complain of severe headache, volunteering at the same time the information that his abdominal pain had ceased; on reexamination he was shown to have slight neck stiffness. His cerebro-spinal fluid, obtained by lumbar puncture, grew a fibrinous web when cold, and contained protein (80 mg. %) and cells (76 lymphocytes and 12 polymorphs per cubic millimetre). A smear showed numerous meningococci. The treatment was changed to intravenous administration of sulphadiazine with hydrocortisone and continued intramuscular administration of penicillin. Nineteen hours after the patient's admission to hospital heavy hæmaturia began. At this point 12 grammes of sulphadiazine had been given in 3·5 litres of N/5 saline during the course of eight hours. Hæmaturia lasted three days, for which time further sulphadiazine therapy was withheld. On the first day a few sulphonamide crystals were found on microscopic examination of the urine, but on the following day none were seen. There were no casts in either specimen; proteinuria was slight and the urine output remained high. Intravenous pyelography performed 31 days after admission gave normal results and the patient was able to leave hospital after 34 days.

Comment.

Abdominal pain has been described early in meningococcal meningitis, being occasionally prominent enough to obscure the true diagnosis (Worster-Drought and Kennedy, 1919). Hæmaturia is also known to complicate the disease (Fairley and Stewart, 1916; Gilchrist and Griffiths, 1954; Tobin, 1956; Worster-Drought and Kennedy, 1919) but there is no mention of association of the two symptoms.

The present case is remarkable for the resemblance of the pain to ureteric colic and the way in which this pain dominated the clinical picture for 17 hours before there was any evidence of meningococcal infection.

The urinary findings make it unlikely that sulphonamides caused the hæmaturia; more probably this was from a septicæmic lesion on the left kidney, the colic arising from clots in the ureter.

Acknowledgements.

My thanks are due to Dr. H. W. Austin and Dr. E. Thompson for their permission to publish this case, and to Dr. G. Pattison for the pathological reports.

References.

FAIRLEY, N. H., and STEWART, C. A. (1916), "Cerebro-Spinal Fever", Commonwealth of Australia Service Publication Number 9: 125.

GILCHRIST, L., and GRIFFITHS, L. L. (1954), "Renal Failure in Meningococcal Meningitis", *Brit. med. J.*, 2: 1337.

TOBIN, J. L. (1956), "Complications of Meningococcus Infection in a Series of Sixty-Three Consecutive Sporadic Cases", *Amer. J. med. Sci.*, 231: 241.

WORSTER-DROUGHT, C., and KENNEDY, A. M. (1919), "Cerebro-Spinal Fever", Black, London: 100.

AN UNUSUAL CAUSE OF MELÆNA.

By H. DONOUGH O'BRIEN, F.R.C.S.I., F.R.A.C.S.,
Burnie,
AND JAMES McG. IMRAY, M.B., Ch.B.,
Hobart.

THE patient, a waterside worker, aged 39 years, was admitted to the Burnie General Hospital on July 14, 1959, complaining of diarrhœa and faintness of 16 hours' duration. Shortly before the onset of symptoms he had had recurrent retrosternal pain in episodes of five minutes' duration, but these had ceased before his admission to hospital. Almost exactly two years previously, on July 18, 1957, he had been admitted to this hospital suffering from cuts about the face, which he had sustained by falling through a glass window when suffering from faintness found to be due to his first attack of melæna. This first attack had been preceded by six months of dyspepsia consisting of pain about half an hour after meals. The first attack of melæna was not accompanied by vomiting or hæmatemesis. The hæmoglobin value was 10·5 grammes per 100 ml. in 1957, and the patient made an uninterrupted recovery from both his cuts and his melæna. A barium meal X-ray examination soon after his discharge showed vigorous peristalsis, but no definite evidence of peptic ulcer. The patient was considered nevertheless to have had a bleeding duodenal ulcer, and was advised as to diet, etc. He adhered to this treatment without symptoms for one year, and then abandoned the diet and continued well until the occasion of his second admission to hospital. He recalled no episodes of melæna, and no recurrence of dyspepsia.

On the present occasion, there was no recurrence of dyspepsia unless the rather minor episodes of retrosternal pain might be so considered, and these had started only just before the melæna. There had been no vomiting or hæmatemesis. The loose motions had been passed during the night, and he had not noted whether they were black; but he felt weak and faint in the morning, and recognized the symptoms from his previous experience.

Physical examination of the patient on his admission gave negative findings except for pallor, and for the presence of tarry black stools in the rectum. The temperature was 97° F., the pulse rate was 90 per minute, the blood pressure was 85/55 mm. of mercury and the hæmoglobin value was 11·2 grammes per 100 ml. He improved temporarily with conservative treatment, but next day it was apparent that bleeding was still occurring, and he was given four pints of compatible group O Rh-positive blood, with symptomatic improvement. However, on the day after this transfusion the hæmoglobin value had gone

down to 10·8 grammes per 100 ml. Melæna continued, and on July 19, five days after his admission, he was given three pints of blood, and the day after, a further two pints; yet the hæmoglobin value was now only 9·0 grammes per 100 ml. During this period a Ryle's tube had been passed and a fractional test meal examination made; this showed a rather high climbing acid curve, but no blood in any specimen.

It was now apparent that surgery was indicated, but the absence of blood in the gastric specimen gave rise to some doubt as to the hæmorrhage being due to a peptic ulcer, so the Ryle's tube was again passed and manipulated into the duodenum, the position being checked radiologically. The duodenal specimen was devoid of blood. The tarry nature of the stools indicated that bleeding must come from fairly high up in the small bowel, and a barium follow-through X-ray examination was considered; but the radiologist visits this hospital only once a week, and the small bowel is notoriously difficult to examine adequately. There was no evidence of cirrhosis of the liver or of blood dyscrasia, although it must be admitted that no special investigation of clotting and bleeding was carried out. There were no petechial hæmorrhages, nor were there arachnoid telangiectases to suggest generalized Osler's disease, and a sigmoidoscopic examination in 1957 had shown no abnormality. Massive and persistent hæmorrhage could be produced from a diverticulum of the colon, but the blood from this level would not be tarry, and the age and build of the patient did not suggest diverticulitis. Regional ileitis must be suspected in a man of this age, but would be unlikely to produce such persistent bleeding in the absence of other symptoms. Hæmorrhage from a Meckel's diverticulum is a common cause of blood in the stools of infants, though not of adults; but Meckel's diverticulum occurs in 1·5% of individuals, so it was with a tentative diagnosis of bleeding from a Meckel's diverticulum that laparotomy was undertaken by one of us (H. D. O'B.) on July 23, nine days after his admission.

Anæsthesia was induced by Dr. J. Taylor with an epidural injection of xylocaine, and narcosis by thiopentone given intravenously and nitrous oxide and oxygen given by inhalation. A right paramedian incision was employed. The stomach and duodenum were normal, but on tracing down the length of the small bowel to a distance of four feet above the ileo-caecal valve, a rather dramatic appearance was disclosed. Unfortunately the clinical photograph was not successful. At the level described, one of the branches of the superior mesenteric artery was enlarged to the size of the radial artery, and ran past the mesenteric border of the gut on to its left aspect where it entered a bright-red, rather raised area some 2 cm. by 1·5 cm., on which were tortuous convolutions of blood vessels of all sizes, drained by a large vein which ran back beside the enlarged artery. About four inches of bowel was resected to include the affected area, and continuity was restored by end-to-end anastomosis. The remainder of the bowel was apparently normal, as was the appendix, which was removed. It was not found necessary to administer the blood which had been held in reserve, and convalescence was uneventful, the patient being discharged from hospital on the eighth day after operation. He was examined again as an out-patient in September, 1959, two months after the operation, when he declared himself perfectly well, the operative scar was soundly healed, and the hæmoglobin value was 14 grammes per 100 ml.

The pathological specimen consisted of four inches of small intestine apparently fed by a large artery which ran to the somewhat thickened area on the left side of the gut. No bleeding point or ulcer was detected macroscopically on the mucosal surface, although there was a tiny dark dot which might have represented the bleeding point. X-ray examination after barium injection of the feeding vessel gave some idea of the appearance.

The sections show a conglomeration of blood vessels, veins and capillaries, and also a few aggregations of cells showing some suggestion of vasoformative activity. The pathologist (Dr. J. T. Quinlan) gave the opinion that the condition was probably a congenital angioma, probably not a true tumour, but a hamartoma.

Discussion.

Hæmangioma of the small bowel is a rare condition. Guy and Cooper in 1950 had recorded 100 cases. Raeford, in a survey, estimated that 8·9% of all gastro-intestinal tumours were small-bowel tumours, and of those 0·3% were hæmangiomas. They appear to be frequently associated with congenital vascular abnormalities elsewhere in the body, and particularly in the skin. P. P. Rickham reports a case of three cavernous hæmangiomas in the ileum associated with a similar cutaneous lesion, and Guy and Cooper's patient had a congenital cavernous hæmangioma of the chest wall along with a solitary hæmangioma one-third of the way down the small bowel. However, in this particular case there was no evidence of a cutaneous lesion.

The following five different types are described (Aird, 1958): (i) multiple phlebectasia, symptomless and rarely causing hæmorrhage; (ii) solitary cavernous hæmangioma, which may be infiltrating or polypoid, and which may give rise to severe hæmorrhage; (iii) capillary hæmangioma with solid elements, giving rise to obstruction or intussusception rather than hæmorrhage; (iv) the tiny telangiectasis associated with generalized arachnoid telangiectasis of Osler's disease; (v) diffuse hæmangiomatosis of the alimentary canal.

The type encountered here does not really fit into any of these categories, except possibly the capillary hæmangioma with solid elements. The tumour did have slight appearances of a mesentery, and in view of its location it is possible that it may have developed from a vestigial Meckel's diverticulum.

The possibility of malignancy must be considered; but malignant change in these vascular tumours is extremely rare (Boyd, 1955). In this case, the pathologist was satisfied that there was no evidence of malignancy in the sections cut.

Acknowledgement.

We wish to thank Dr. J. T. Quinlan for his pathological report on the specimen.

References.

AIRD, I. (1958), "Companion in Surgical Studies", Livingstone, Edinburgh: 844.

BOYD, W. (1958), "Textbook of Pathology", Lea & Febiger, Philadelphia: 261.

GUY, C. C., and COOPER, H. F. (1950), "Solitary Hemangioma of Small Intestine", *Surgery*, 27: 93.

RAIFORD, T. S. (1932), "Tumors of Small Intestine", *Arch. Surg.*, 25: 122, 321.

RICKHAM, P. P. (1952), "A Case of Hæmangiomatosis of the Small Intestine", *Brit. J. Surg.*, 39: 462.

Reviews.

The Care of Minor Hand Injuries. By Adrian E. Flatt, M.A., M.D., F.R.C.S.; 1959. St. Louis: C. V. Mosby Co. Price: £5 4s. 6d.

THIS is a book about hand injuries which normally would not require the patient to be admitted to hospital—injuries in which there is sustained a small amount of tissue loss. Out-patient treatment can be given, and they are usually free of post-operative complications.

The book is arranged in two main parts. The first is entitled "General Principles of Care". It includes chapters on anatomy, the principles of care, surgical techniques and the classification and examination of injuries. The second part deals with the care of specific injuries, and all types are considered in full detail. The chapters here are on wounds of the skin, injuries to the nail, pulp loss, amputation, crush injuries, tendon injuries, joint injuries, fractures, burns, infections and miscellaneous injuries and wounds.

In the preface the author asks even the most conscientious reviewer not to attempt to read this second part as a whole. It has been arranged so that when an injury is seen the appropriate chapter can be consulted, and this chapter will give a fully detailed account of the treatment, without any

need for repeated reference to previous chapters. This, of course, has required a considerable amount of repetition. The book has been used in the suggested manner over the past few months and has been found extremely useful.

The author has described those methods of treatment, and only those methods, which he has found to be effective, consequently we think that in some of the chapters other methods of treatment than those given may be more effective. Such differences of opinion are to be expected, and this in no way detracts from the excellence of the book. It is well written, beautifully illustrated and strongly bound. The young surgeon or casualty officer will find here all the little details which, all too often, he has to learn from bitter experience. It should be available in the casualty departments of all hospitals and would be a most valuable addition to any young surgeon's library.

Surgical Treatment of Trauma. Edited by Preston A. Wade, M.D., with 35 contributors; 1960. New York and London: Grune & Stratton. 9¼" × 6¾", with illustrations. Price: $26.50.

THIS book is compiled of revised lectures delivered by members of the Cornell University Medical College during an annual post-graduate course. The topic common to all is trauma, which is covered by 25 different authors. An attempt has been made to present personal viewpoints and to eliminate, what is so common in many American books, valueless reviews of historical matters long since put to rest. Each lecturer has been asked to present his subject in his own instructing method.

Though it may be an admirable objective to avoid excessive conformity of the text, it does in fact cause some of the chapters to be loosely written and ill composed. Most traumatic subjects are covered, including bony and soft-tissue trauma, and the specialties, including head, facial bones, vessels, thorax and abdomen. Few, if any, of the chapters can be read profitably without a considerable prior knowledge of the subject, and attitudes or approaches are more stressed than the minutiæ of technique and management. Much of the emphasis in the treatment of bony trauma by pins and various metallic foreign bodies cuts across traditional English practice.

This is an interesting book to dip into as a record of current practice in one American hospital; but it is no more than that.

The Principles and Practice of Medicine: A Textbook for Students and Doctors. By Sir Stanley Davidson, B.A., Cantab., M.D., F.R.C.P. Edin., F.R.C.P. Lond., M.D Oslo, F.R.S. Edin.; fifth edition; 1960. Edinburgh and London: E. & S. Livingstone Ltd. 8½" × 5", pp. 1128 with many illustrations. Price: 35s. (English).

IN the preparation of the fifth edition of this book, the editor has been careful to preserve the original policy—namely, to concentrate on disorders "most commonly encountered in practice". The space merited by rarer diseases is governed by their cultural interest or educational value "as examples of applied anatomy or physiology".

No major changes distinguish the new edition. Although 45 pages longer than the previous one (owing to the inclusion of new material in almost every section—for example, a discussion of tranquillizers and other drugs in the section on psychological medicine), the book is streamlined by the deletion of material which the author deemed redundant or out of date. Always a very popular book among students, it is nevertheless insufficient for the needs of most of them, and can best be described as an introduction to a more intensive study.

Radiation Injury in Man: Its Chemical and Biological Basis, Pathogenesis and Therapy. By Eugene P. Cronkite, M.D., and Victor P. Bond, M.D., Ph.D.; 1960. Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 9" × 5¾", pp. 208. Price: 52s. (English).

THE authors believe that the medical profession in general has not yet accepted its responsibility for evaluating the extent of the hazards of radiation to man, and that by default less-qualified individuals from other disciplines have been able to predict dire consequences and present unbalanced and misleading statements without contradiction. Further, they believe that the medical profession must recapture this lost ground and retain responsibility for safeguarding the public in this essentially preventive medicine sphere. The authors, both actually engaged in radiobiological research since the war and well qualified to write on this subject, have fulfilled their aim in writing a book which can easily be interpreted by the non-specialist and the student entering this specialized radiological field. Continuing simplicity of presentation is apparent throughout the compact work. It follows the pattern of most of the recent books encompassing somewhat the same subject in giving half the text to explaining radiation physics and the biological action of radiation, so that the remainder of the book dealing with radiation injury can be properly understood. The text is only some 170 pages in length, free of verbiage and so laid before the reader that one question leads naturally to the next, making a coherent readable whole. One-quarter of the bibliography of about 100 major scientific articles refers to work by one or other of the authors, emphasizing their wide experience of the field and their ability to offer the facts and the arguments, suitably digested, to a reader wishing for an easy introduction to what is too often considered a difficult subject.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Respiration: Physiologic Principles and their Clinical Applications", by P. H. Rossier, A. A. Bühlmann and K. Wiesinger, edited and translated from the German edition by Peter C. Luchsinger, M.D., and Kenneth M. Moser, M.D.; 1960. St. Louis; The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Ltd. 9¾" × 6¼", pp. 504, with 95 illustrations. Price: £8 13s. 3d.

"Eugene Wolff's Anatomy of the Eye and Orbit: Including the Central Connections, Development and Comparative Anatomy of the Visual Apparatus", revised by R. J. Last; fifth edition; 1961. London: H. K. Lewis and Co. Ltd. 9¾" × 7", pp. 508, with 438 illustrations. Price: £4 4s.

"The Year Book of Drug Therapy (1960-1961 Year Book Series)", edited by Harry Beckman, M.D.; 1961. Chicago: The Year Book Publishers Inc. Melbourne: W. Ramsay (Surgical) Ltd. 7½" × 5½", pp. 588. Price: £4 13s. 6d.

"The Year Book of Obstetrics and Gynecology (1960-1961 Year Book Series)", edited by J. P. Greenhill, B.S., M.D., F.A.C.S., F.I.C.S. (Honorary); 1961. Chicago: The Year Book Publishers Inc. Melbourne: W. Ramsay (Surgical) Ltd. 7½" × 5½", pp. 576. Price: £4 8s.

"The Year Book of General Surgery (1960-1961 Year Book Series)", edited by Michael E. De Bakey, B.S., M.D., M.S., with a section on "Anesthesia" edited by Stuart C. Cullen, M.D.; 1961. Chicago: The Year Book Publishers Inc. Melbourne: W. Ramsay (Surgical) Ltd. 7½" × 5", pp. 616, with many illustrations. Price: £4 8s.

"The Year Book of Ophthalmology (1960-1961 Year Book Series)", edited by William F. Hughes, M.D.; 1961. Chicago: The Year Book Publishers Inc. Melbourne: W. Ramsay (Surgical) Ltd. 7½" × 5", pp. 376, with illustrations. Price: £4 13s. 6d.

"Annual Review of Medicine, Volume 12, 1961", edited by David A. Rytand, M.D.; 1961. California, Palo Alto: Annual Reviews, Inc. 9" × 6¼", pp. 464. Price: $7.50.

"Somatic Treatments in Psychiatry: Pharmacotherapy; Convulsive, Insulin, Surgical, Other Methods", by L. B. Kalinowsky, M.D., P. H. Hoch, M.D., and B. Grant, M.D., D.P.M.; 1961. New York: Grune & Stratton, Inc. 10" × 6¼", pp. 414. Price: $9.75.

"The Day Hospital Movement in Great Britain: An Analysis and Description of Sixty-Five Day Hospitals and Day Centres with Special Reference to Psychiatric and Geriatric Day Hospitals Visited in 1958-9", by James Farndale, B.Com., F.H.A., M.R.S.H.; 1961. Oxford, London, New York, Paris: Pergamon Press. 9" × 6", pp. 448, with illustrations. Price: 84s. net (English).

"Textbook of Pathology: An Introduction to Medicine", by William Boyd, M.D., Dipl. Psychiat., M.R.C.P. (Edin.), Hon. F.R.C.P. (Edin.), F.R.C.P. (Lond.), F.R.C.S. (Can.), LL.D. (Sask.), (Queen's), D.Sc. (Man.), M.D. (Oslo); seventh edition, thoroughly revised; 1961. Philadelphia: Lea & Febiger; Sydney: Angus & Robertson. 10" × 7", pp. 1370, with illustrations. Price: £9 18s.

"Molluscicides: Second Report of the Expert Committee on Bilharziasis", World Health Organization Technical Report Series No. 214; 1961. Geneva: World Health Organization. 9¼" × 6¼", pp. 50. Price: 3s. 6d.

"The New Guinea Offensives", by David Dexter; Australia in the War of 1939-1945, Series One: Army, Volume 6; 1961. Canberra: Australian War Memorial; Sydney: Angus & Robertson Ltd. 9¼" × 6", pp. 870. Price: 40s.

The Medical Journal of Australia

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INFLUENZA PANDEMICS.

IT seems that the great influenza pandemics occur about once every generation. Their dramatic appearance bestirs medical science and public health authority to action, but interest soon wanes. The lessons learned are quickly forgotten, and each fresh pandemic presents a series of new problems. In view of this "traditional pattern", the U.S. Public Health Service recently established an Advisory Committee on Influenza, whose first recommendation was to hold an International Conference on Asian Influenza. This Conference took place extending over three days, in February of last year, in Bethesda, Maryland, and was attended by representatives from England, Holland, Japan, Switzerland and Russia, in addition to over 80 top-line American scientists. The proceedings were deemed of sufficient importance to be published as a special number of the *American Review of Respiratory Diseases*, occupying 220 pages.[1] A quotation from the foreword gives a fair appraisal of its worth: "This Conference has resulted in a significant contribution to the knowledge of influenza, and it is believed that this report will represent a reference work for years to come. Within the pages of these proceedings dramatic evidence may be found of more precise epidemiologic, clinical and basic research." Anyone interested in influenza—and who is not?—could browse through these proceedings with pleasure and profit (there are no long papers), while for many they will be required reading.

It is not possible to summarize the entire conference, but certain aspects merit comment, particularly those which may bear on Australia's position in relation to these great pandemics. It seems that this epidemic had its origin in Central China, but it became known to the rest of the world only when it spread to Hong Kong and Singapore in April, 1957. Studies in Washington, London and Melbourne (Burnet) soon identified the causal virus as being distinct from the hitherto prevalent A1 strain. It belonged "to a new set of type A variants, composed of a significantly different antigenic strain". (Historically, it was noted that an influenza virus had been first isolated 25 years previously.) It was immediately recognized that the long-expected new pandemic virus had emerged, and its spread was predicted with great accuracy, through South-East Asia, to the Southern Hemisphere, and later to the Northern Hemisphere. The dominant fear in the minds of medical authorities and others was that this virus, soon to be given the appelation of A2, also known as A/Asian, would result in a universal holocaust, as in 1918. In the event of course, as a result of good fortune and not good management, it did not. The incidence was much greater than in other recent epidemics, but the mortality was not. By and large, about 50% of populations was affected, the most susceptible group curiously being that from 5 to 19 years of age, incriminating the school as a more important source of dissemination than the home. One speaker at the conference pointed out, however, that only about 50% of so-called influenza was actually due to the influenza virus: at least 15 other viruses could cause similar symptoms. Most deaths occurred in persons over 65, and it was noted that secondary staphylococcal infection was relatively common and of course most serious in some communities. The veterinarians made an interesting contribution, presenting evidence that some animals were naturally susceptible to human influenza virus, and suggesting the possibility of animal reservoirs existing in nature, as an endeavour of the virus to perpetuate itself. Several important papers were presented at the conference on virus isolation, serological diagnosis, the hæmadsorption technique and fluorescent antibody staining; these should repay study by laboratory workers. Reference was made to a world-wide system of laboratories designed to forward immediately to the two chief centres of virology, namely, the National Institute of Research, Mill Hill, England, and the Communicable Diseases Centre, Atlanta, Georgia, not only influenza viruses which may be novel, but other respiratory viruses which appear to be new. The importance of influenza research, in the respiratory field and of course in virus research generally, was made manifest. It was stated incidentally that there were 6 of these laboratories in Australia, 29 in Europe, 11 in Asia and 7 in Africa.

The possibility of effective widespread vaccination was discussed at length, and indeed this may well be the most valuable practical outcome of the conference. It was not disputed that useful vaccines were available, or that more effective ones would eventually be produced. And it was agreed that tremendous advances had been made recently in immunological knowledge, including the efficacy of vaccination. But there was a rather sharp difference of opinion in regard to the best type of vaccine to use at present. For instance, Dr. C. H. Andrewes, the leading English authority, urged that only a strain-specific vaccine was worth while, and that it was useless to stockpile a polyvalent vaccine against a future outbreak. The Americans, led by Dr. T. Francis Junior, also a pioneer in influenza virology, maintained that this was a defeatist attitude, and that a vaccine compounded of each of the four families of virus A and the two families of virus B should be built up in readiness. It was pointed out that in the 1957 epidemic in the United States, supply fell far short of demand at the peak period despite tremendous efforts, only 15,000,000 doses having been available and distributed just prior to the

[1] *Amer. Rev. Resp. Dis.*, 1961, 83, No. 2, Part II (February).

peak. The inference was that a stock vaccine would be of great value despite its non-specificity. Dr. Andrewes' somewhat crushing reply was that "all successful vaccinations that I have ever read of have been done using an antigen made with a current strain". It is of interest to note here that the vaccine in current usage in Australia contains seven different strains, including the Asian variety.

Other matters on which finality was not reached included the use of mineral oil emulsion as an adjuvant, the choice of route of injections, whether intracutaneous, subcutaneous or intramuscular, and the frequency of repetition of administration. Mention was made of the economics of vaccine production, a costly process on a large scale. Priorities were discussed in terms of essential personnel, age, preexisting disease and pregnancy, which together one speaker thought might involve some 20% of an entire population, and it was recognized that improper allocation and slow distribution might nullify all laboratory efforts. Of interest was one paper dealing with the lack of concern generally with the possibility of vaccination against influenza. A mass survey indicated that though the public believed vaccination was valuable, few regarded influenza as more serious than a common cold; hence they were not concerned to seek prophylaxis. Surprisingly, this opinion was shared by most medical society officials. That they were mainly correct in this laissez-faire attitude was fortuitous, though fortunate, the point being that vaccination must be undertaken about a month before the incidence wave. To attempt mass vaccination at the peak period is futile; when panic sets in it is far too late to shut the stable door. It was agreed that there was need both for educating the public in the value of influenza vaccine and also for informing them of the imminence of an epidemic and of the measures to be taken to cope with it.

An outstanding paper from a practical aspect was that of the Surgeon-General of the U.S. Public Health Service, Dr. L. E. Burney, on their "preparedness plans" for the next pandemic. He enumerated four categories: (i) Recognition of the pandemic, (ii) preparation of vaccine, (iii) use of vaccine and its distribution, together with dissemination of information, (iv) continuing research. Wisely, he conceded the differing viewpoints of physician and public health officer, the former concerned with protecting his own individual patients, the latter with protecting those whose continued activities are essential to the community. For this group, by the way, Dr. Burney gives the figure of 6,000,000 in the United States, a much lower figure of course than the combined priorities quoted earlier. His short paper should be read in full, but his final remarks merit quotation here. For his successor in office when the next pandemic strikes he hopes to provide "three different kinds of sound investments. They are (1) a finite set of operating plans based on the experience of 1957, (2) a continually accumulating body of scientific information resulting from sound research on influenza . . . (3) a group of senior scientists and health officers who have maintained an acquaintance with the field and who can serve as his advisors".

It is to be hoped that a comprehensive plan such as this is part of the programme of the Commonwealth Department of Health. Perhaps some modification of it could be followed with advantage. But it would need the cooperation of everyone. It is understood, for example, that in 1957 the N.S.W. Minister for Health established an Advisory Committee on Influenza, which recommended vaccination to selected groups.[2] This is a valuable commencement; but it must be supplemented by the Commonwealth, in ways such as those indicated by the U.S. Surgeon-General. On the other hand, the Commonwealth must be able to look for cooperation from the States, and both must be able to rely on the practising medical profession if effective machinery is to operate. It may not be generally known that in 1951 the World Health Organization designated the Commonwealth Serum Laboratories an Influenza Centre with obligations (i) to ascertain and report to the World Health Organization upon the occurrence of influenza in Australia, (ii) to identify strange viruses associated with epidemics, (iii) to forward strains of virus to the appropriate laboratory, and (iv) to train staff for these purposes in various areas in Australia. The ideas behind this procedure are, firstly, to give time and warning to Australia and other countries regarding the rate and direction of the spread of epidemics and, secondly, when a particular Australian virus is involved, to permit the time for preparation of an appropriate vaccine in sufficient amount to protect the population in unaffected regions in the country. The information which needs to be supplied includes (i) notification of the occurrence of influenza in respect of time and place, (ii) details of its incidence, effect on industry, etc., (iii) the degree of severity, the occurrence of complicating pneumonia and mortality, and (iv) identity of the virus. If the Commonwealth Serum Laboratories are to discharge their obligations to the World Health Organization and, looking in the other direction, to Australia, they must be supplied with early intelligence concerning influenza. This implies not only prompt return of the information required but the forwarding of specimens, when requested, to permit the isolation and identification of the virus. This routine is of far more than academic interest. It is a responsibility of Commonwealth and State departments to avert an epidemic in Australia comparable to that of 1918-1919, and the only means readily available depends on prompt recognition of early cases and timely identification and culture of the particular virus involved. This places on the States the obligation to keep the incidence of influenza under close scrutiny and to supply the necessary materials from patients to the Commonwealth Serum Laboratories. It requires greater vigilance than with the usual run of notifiable diseases. Inclusion of influenza in the list of routinely notifiable diseases is not usual in most States of Australia, and this is understandable. The term is found convenient by many practitioners as a label for many vague transient febrile illnesses, and information obtained from compulsory notification all the year round could have little value. Nor would it evoke much cooperation from the practising profession. When

[2] *Health in N.S.W.*, 1961, 2: 10 (May).

the occasion warrants it, however, the fullest cooperation in the notification of influenza with the supply of detailed information can be reasonably asked for and can be expected. Influenza thus presents a nice example of the importance of the spirit rather than the letter of notification procedure.

Comments and Abstracts.

CIGARETTE SMOKE AND THE DRAINAGE OF THE BRONCHIAL TREE.

THE sound and the fury of the debate on whether smoking causes lung cancer continue unabated. Whilst most scientists and physicians who have studied the subject agree that the association between them is one of cause and effect, a small "hard core" remains not only unconvinced, but, in some cases, quite emphatic that there is no evidence at all relating the two. The last-mentioned group is a source of great comfort to "addicts" and to vested interests. It is refreshing therefore, to turn to a paper by an American professor, A. C. Hilding of Minnesota,[1] who has made a special study of this subject for more than thirty years, wherein he blandly discusses not whether but just why cigarette smoke causes squamous-cell carcinoma of the respiratory tract. No element of doubt enters his mind, secure in the knowledge that the tar in this smoke contains carcinogens, a fact no one now denies. The completely objective reader, if any there be on a subject which has such an emotional content, may be disposed to agree that this author has really "got something".

Hilding's theory, derived from an extensive study of the physiological drainage of the bronchial tree, is a simple one. Inhaled cigarette smoke, he points out, by-passes the natural cleansing mechanism of the nose, to which most air pollutants are subjected. The tar droplets from the smoke are diffusely deposited in the mucous layer covering the tracheo-bronchial tree as the inspired air flows down. The greatest total quantity is deposited in the small bronchioles and alveoli, by virtue of their great mass surface area. Drainage of the bronchi is accomplished by the "mucous blanket" which, moved along by the cilia, constitutes the ciliary stream. In its ever-narrowing course upwards, the ciliary stream encounters a number of naturally occurring obstructions, in the form of squamous islands and bronchial openings. The ciliary stream is retarded at these sites. Further, cigarette smoke, possibly through its nicotine content, has been shown to slow down or temporarily stop ciliary action. This would further delay ciliary flow and correspondingly increase invasive or destructive action of any noxious agent, especially at the obstructing sites. Squamous cell carcinoma is believed to have its genesis in the squamous islands in many cases, and the invocation of the upward flowing carcinogen-carrying ciliary stream as a factor is an ingenious and plausible hypothesis, which reverses the widely held belief that it is the smoke going down that counts, and not what comes up, dredged as it were, from the lower tract. It would answer the criticism, for instance, that carcinoma of the larynx and trachea should be more frequent than that of lower bronchi if cigarette smoke is a cause. All in all, it is a theory which appears to have considerable merit.

THE OUTLOOK IN RHEUMATIC FEVER.

TWENTY YEARS AGO J. D. Keith,[1] of Toronto, published a paper on the prognosis of rheumatic heart disease which took into account most or all of the important surveys which had been conducted at that date, and provides an authoritative account of the outlook before the advent of steroids and of the prophylactic use of antibiotics. Keith now returns to the subject with a review[2] of modern trends in acute rheumatic fever which gives a useful account of the situation as it stands at present. He begins by noting the diminished importance of rheumatic heart disease in the pædiatric age group, which he attributes to the decline in the incidence of streptococcal disease, to the improved social and economic conditions of the population, and to increased awareness of the large number of cases of congenital heart disease. He remarks that it is being realized for the first time that in childhood congenital heart disease is approximately ten times as common as heart disease of rheumatic origin.

Confirmation of a decline in both the incidence and severity of rheumatic heart disease comes from a wide variety of sources. Keith states that 20 years ago it was generally considered that rheumatic heart disease occurred in approximately 2% of the school population, whereas several recent surveys show an incidence of about 0·3%. Studies of streptococcal epidemics among service personnel in the last war demonstrated the development of rheumatic fever in about 3% of cases. Since it may be assumed that almost all children experience one or more streptococcal infections during childhood, it seems clear that the incidence of rheumatic fever after such infections is probably only about a tenth of that quoted for war-time outbreaks in an adult population. This discrepancy may perhaps be explained by postulating that streptococcal strains responsible for epidemics are virulent ones which have a high rheumatic potential, whereas sporadic cases are caused by a great variety of strains, many of which may have little tendency to cause rheumatic complications.

As regards the treatment of rheumatic fever, the most important changes in the past 20 years have of course been the introduction of the use of hormones and antibiotic therapy. The findings of the International Co-operative Study, in which American, British and Canadian investigators cooperated in a clinical trial of ACTH, cortisone and aspirin in the treatment of rheumatic fever, still tends to dominate the picture. Their first report, published in 1955, showed that there was little to choose between the three treatments as far as the evolution of the disease was concerned. The incidence and persistence of residual cardiac damage was essentially the same in all groups. This result has received further confirmation from the five-year follow-up report of the study, published simultaneously in the *British Medical Journal*,[3] in *The Canadian Medical Association Journal* and in *Circulation* in the United States. An important point emphasized in this latest report is that the major factor which determines the incidence of rheumatic heart disease at the end of five years after the initial attacks is the status of the heart at the time treatment was begun. Keith, who is the principal Canadian representative in this study, points out in his own article that several other studies on the relative merits of hormones and salicylates have now appeared. Some of these present findings which suggest that the hormones are superior to salicylates. In an important study from Sheffield, R. S. Illingworth and his colleagues[4] found that cortisone was superior to salicylates, but that the combination of both together was better than either alone. Keith concludes that both hormones and salicylates have a useful place in the treatment of acute rheumatic fever. Hormones are particularly useful in the early stages. Nodules and murmurs disappear more rapidly with hormonal therapy, and the conduction time of the electrocardiogram regains its normal value more quickly. On the other hand salicylates are particularly valuable in the later stages. Their use prevents the rebound phenomena sometimes noted after hormone therapy is stopped, and with salicylates, as opposed to hormones, it is possible to use the sedimentation rate as a guide to the activity of the rheumatic process.

[1] *Dis. Chest*, 1961, 39:357 (April).
[1] *Canad. med. Ass. J.*, 1941, 45:119 (August).
[2] *Canad. med. Ass. J.*, 1960, 83:789 (October).
[3] *Brit. med. J.*, 1960, 2:1033 (October 8).
[4] *Lancet*, 1957, 2:653 (October 5).

Keith therefore suggests that, since the effects of hormones and salicylates are not identical, it is reasonable to give them together from the beginning of the illness. He recommends that 50 or 60 mg. of prednisone should be given daily for one week, with a gradual scaling down of the dose during the next week until it is eliminated entirely, and that at the same time salicylates should be given in a dosage of one-half to two-thirds of a grain per pound body weight in every 24 hours; this should be kept up for several weeks until after the sedimentation rate has become normal.

In a discussion of antibiotic therapy, Keith brings forward evidence that penicillin therapy is not only valuable in preventing rheumatic fever when used for hæmolytic streptococcal infections, but is also useful in lowering the incidence of heart disease, when given in the early stages of rheumatic fever. He quotes the work of Mortimer, Rammelkamp and their associates, though he does not subscribe to their hypothesis that valvulitis may be caused by a bacterial infection in the heart valve itself. Keith considers that the beneficial effect of penicillin is due to the elimination of streptococci from the upper respiratory passages; many patients with acute rheumatic fever are still harbouring virulent streptococci, and it is logical to suppose that their eradication will help in combating the disease of which their presence is the cause. Keith therefore proposes an injection of 1,200,000 units of benzathine penicillin once a week for three weeks during the acute phase of the disease, and therafter once a month as prophylaxis against recurrence.

Some views on the prophylaxis of rheumatic carditis were discussed in these columns recently,[5] so it is sufficient to note here that Keith favours monthly injections of a long-acting penicillin. He believes that the superiority of this method lies in the fact that only two-thirds or three-quarters of patients given penicillin to be taken orally do so with suitable regularity, and that the large monthly dose not only suppresses infection but effects a complete clearance of streptococci from the throat at regular intervals.

Finally, Keith discusses the prognosis in acute rheumatic fever. He notes the evidence that this is improving in each decade, and states:

> mortality is falling, recurrences are less common, initial attacks appear to be less severe, streptococcal disease is more readily treated, and surgery for valvular stenosis or incompetence is becoming progressively better.

As marshalled by Keith, the evidence strongly suggests that much of this improvement is due to the introduction of effective anti-streptococcal therapy and a better understanding of its application, and that the introduction of steroid therapy has been of relatively minor importance.

SHORTER ABSTRACTS.

OPHTHALMOLOGY.

ASPIRATION OF CONGENITAL OR SOFT CATARACTS. H. G. Scheie, *Amer. J. Ophthal.*, December, 1960.

THE author reviews the various methods used in the treatment of congenital cataracts and describes in detail his new technique of aspiration. When the cataract is complete, a small conjunctival flap is reflected towards the limbus. A superior rectus suture is placed. The eye is fixed at the 6 o'clock position and a Ziegler needle is inserted 1·5 to 2·0 mm. behind the limbus. A wide cruciate incision is made in the capsule and the needle withdrawn. A special thin-walled number 19 needle with an oval tip is inserted, bevel down, through the knife-needle incision. It is attached to a 2 ml. syringe containing 0·25 ml. of saline. When the tip of the needle is at the lower pupillary border the needle is rotated so that the bevel faces the cornea and suction is created by wthdrawing the plunger. When the chamber is clear the needle is withdrawn. The scleral incision is closed with catgut suture and finally the conjunctiva is closed. When there is an incomplete cataract a large cruciate incision is made in the capsule and some days later aspiration is performed. If the pupil does not dilate widely, then an iridectomy can be performed by enlarging the knife-needle incision to 2 or 3 mm., the iris is made to prolapse and teased out by hand-over-hand action with iris forceps, and a complete iridectomy performed.

POST-OPERATIVE INTRAOCULAR INFECTIONS. I. Leopold and L. Apt, *Amer. J. Ophthal.*, December, 1960.

THE authors discuss various aspects of intraocular infection. Most intraocular infections are caused by staphylococci, streptococci, pneumococci, *Escherichia coli*, *Pseudomonas æruginosa* and *Proteus* species. Fungous infections are being reported, and it is said that their increased frequency is due to the use of antibiotics and steroids for other purposes. The source of infection and methods of prevention of intraocular infections are discussed. Drugs used in active therapy of intraocular infection are classified as bactericidal or bacteriostatic. The former are penicillin, bacitracin, ristocetin, vancomycin, streptomycin, polymyxin B, neomycin, kanamycin, colistin and furaltadone; the latter are erythromycin, oleandomycin, spiramycin, novobiocin, carbomycin, the tetracyclines, chloramphenicol, soframycin, amphotericin B and the sulphonamides. The authors regard chloramphenicol as an appropriate drug with which to initiate therapy because it diffuses well into the intraocular tissues and fluids and has a wide spectrum of antibacterial activity. Their order of preference for systemic therapy against unidentified micro-organisms is chloramphenicol, kanamycin, penicillin with streptomycin and a tetracycline. As part of initial therapy subconjunctival injection is also recommended with, in order of preference, neomycin, bacitracin with polymyxin B, erythromycin, novobiocin, or penicillin with streptomycin. Treatment with a different antibiotic with corticosteroid is initiated if there is no improvement in 24 hours and this is based if possible on bacteriological studies. The authors describe each drug individually and discuss also the value of various anti-inflammatory agents.

UNILATERAL PAPILLŒDEMA. E. B. Dunphy, *Amer. J. Ophthal.*, December, 1960.

THE author reviews the causes of unilateral papillœdema, and discusses them as due to ocular orbital pathology and as due to intracranial pathology. Congenital abnormalities may produce a picture resembling papillœdema, but which is in fact a pseudopapillœdema. Unequal pressure in the two eyes and sudden lowering of the intraocular tension may produce papillœdema. Posterior uveitis may also produce papillœdema by extension of the inflammation to the nerve head. Inflammation of the optic nerve and optic nerve tumours may produce papillœdema. Obstruction of the central retinal vein may produce swelling of the nerve head. Orbital infections rarely cause papillœdema. Cerebral tumours, especially meningioma of the sphenoidal ridge, may produce optic atrophy in one eye and papillœdema in the other. Brain abscess and intracranial vascular anomalies may both on rare occasions produce unilateral papillœdema.

THE DEVELOPMENT OF OPHTHALMIC ANÆSTHESIA. W. S. Atkinson, *Amer. J. Ophthal.*, January, 1961.

THE author traces the history of anæsthesia with particular reference to its use in ophthalmology. When he comes to present day techniques he favours pre-anæsthetic medication which should render the patient amnesic, but still mentally cooperative with a feeling of unconcern in regard to the operation. For anæsthesia the authors prefers "Xylocaine", 2% solution, with 1:100,000 adrenalin; to this is added hyaluronidase, 6 units per ml. To produce anæsthesia of the orbicularis muscle, the author describes a technique in which the injection is given at the inferior edge of the zygomatic bone in line with the lateral margin of the orbit. The needle is directed up, close to, and across the zygomatic bone at an angle of 30° from the vertical, and 3 or 4 ml. of anæsthetic are injected as the needle advances. Retrobulbar injection should be followed by pressure and massage until the eye is soft and the pressure should be interrupted frequently to avoid interference with retinal circulation. The author prefers local anæsthesia and considers that general anæsthesia is indicated for babies and young children, for extensive operations in adults such as removal of orbital tumours, exenteration and some plastic

[5] MED. J. AUST., 1960, 2: 866 (November 6).

operations, for patients who object to local anæsthesia and for some mental patients. There are more complications when intraocular surgery is done with general anæsthesia than with local anæsthesia, yet some ophthalmologists still employ general anæsthesia routinely.

CONGENITAL HEREDITARY CORNEAL DYSTROPHY. A. E. Maumenee, *Amer. J. Ophthal.*, December, 1960.

THE author describes eight patients with congenital hereditary corneal dystrophy. The condition is usually present at birth but may not be noted by the parents for a month or so. The degree of corneal clouding varies from almost complete opacification to a slight haze and both eyes are usually equally involved. The epithelium is frequently roughened but it does not stain. The stroma is diffusely œdematous. The cornea is avascular and sensitivity is normal. The condition has to be differentiated from congenital glaucoma, birth injury with rupture of Descemet's membrane and intrauterine inflammation. Histological examination of a corneal button removed during keratoplasty showed a diffuse œdema of the corneal stroma. In spite of the diffuse œdema of the cornea, it does not become vascularized, even when present for many years.

OTO-RHINO-LARYNGOLOGY.

CONGENITAL DEHISCENCE OF THE FALLOPIAN CANAL IN MIDDLE EAR SURGERY. J. Kaplan, *Arch. Otolaryng.*, August, 1960.

THE author reports the finding of this congenital condition during middle-ear surgery for otosclerosis. Only cases of pure otosclerosis were considered in this series; that is, where infection had been a factor, that case was excluded. The series included 100 consecutive cases and the dehiscence was found in seven of these cases. With the advances in technique of middle ear surgery, this finding becomes increasingly important to the otologist who embarks on this type of surgery. The author quotes Shea as stating that the dehiscence might occur as frequently as in 25% of cases. The dehiscence is, as a rule, oval in shape and generally above the oval window niche. It usually has smooth edges. Palpation with a blunt-topped instrument is necessary to make a definite finding; this causes the underlying facial nerve to quiver characteristically. The author suggests a reason for this congenital abnormality.

AN OPERATIVE METHOD GIVING SATISFACTORY RESULTS IN THE TREATMENT OF OZENA. U. Siirala, *Arch. Otolaryng.*, August, 1960.

THE author points out the variety of methods which have been employed in treatment of this condition, that none have been very effective, and that when the ætiology is more clearly understood the possibilities of preventing, in advance, the development of the disease will probably be better. Attempts to narrow the enlarged nasal airways have been the usual surgical methods employed in treatment. Numerous types of implants have been tried. The author suggests that dolomite has properties which make it admirably suited for this purpose. The dark dolomite quarried in Finland is for practical purposes non-absorbable as well as being well tolerated, easily shaped and unaffected by boiling for sterilization. It is also easily seen in X-ray films. The pieces are made into rod shapes and inserted submucoperiosteally through incisions made in the nasal vestibule. Thus they can be placed either on the septal side, lateral wall or floor of the nasal cavity.

TYMPANOSCLEROSIS. W. F. House and J. L. Sheehy, *Arch. Otolaryng.*, September, 1960.

THE authors describe tympanosclerosis as a sclerotic or hyaline change in the mucous membrane of the middle ear and mastoid. Known for many years as chalk patches of the tympanic membrane, it is only recently, with the growing interest in reconstructive middle ear surgery, that its clinical significance has been recognized. It is to be differentiated from cholesteatoma and otosclerosis which it may mimic. The name was coined by Zöllner, who states that von Tröltsh described "sclerosis of the tympanic tissue" in 1873. The condition may be spread throughout the tympanum but may be localized to (i) the epitympanum, surrounding the ossicles in a thick sclerotic mass; (ii) the fossa ovalis, partially or completely filling the niche; or (iii) the eardrum, appearing as chalk patches (the only site where it can be seen pre-operatively). It occurs after repeated bouts of inflammation, and there is invasion of the tunica propria of the mucous membrane of the middle ear by fibroblasts with organization of the tunica into a thick collagenous connective tissue. Hyaline degeneration occurs. The process takes place between the epithelium and periosteum and destroys neither. The authors point out that, from a practical clinical point of view, the distinction from cholesteatoma and otosclerosis is important if maximum hearing gain is to be obtained in middle ear surgery.

CARCINOMA OF THE LARYNX AFTER IRRADIATION FOR PAPILLOMA. T. C. Galloway *et alii*, *Arch. Otolaryng.*, September, 1960.

THE authors discuss the use of irradiation in a case of laryngeal papilloma in which carcinoma developed later. They state that, whilst it is not possible to prove positively that the radiation was responsible for the malignant change, the presumption is very strong. They state that Goolden's criteria of histologically proven carcinoma occurring in a previously irradiated area after a suitable period of time and at an age earlier than normally expected are fulfilled. The case described is that of a eight-year-old boy who had laryngeal papillomas and whose larynx was irradiated. Carcinoma was found when biopsy was performed 28 years later. The opinions of various authors regarding the problems which arise in this case are discussed, such as whether papillomas of this type do tend to produce a malignant state later if exposed to certain types of irradiation. They conclude that irradiation is a cause of carcinoma in the larynx in a case such as this and that it should not be used for benign conditions in which other treatment is adequate.

TRACHEOTOMY IN POLIOMYELITIS AND SIMILAR DISEASES. J. E. Allen and C. S. Blase, *Arch. Otolaryng.*, October, 1960.

IN 1954, the authors presented a guide for the use of tracheotomy in cases of poliomyelitis and other conditions where it would be necessary. This guide has been used successfully since that time. Whilst admitting the usefulness of laboratory estimation, they state that the grounds for tracheotomy are clinical. The tracheotomy accomplishes two purposes. First it by-passes the laryngeal obstruction due to vocal cord paralysis or collapse of supporting neck muscles, and secondly it permits removal of secretions obstructing air flow to the lungs. The groups requiring tracheotomy are stated to be: (*a*) those with simple respiratory muscle paralysis; (*b*) the bulbar group, with tenth cranial nerve involvement; (*c*) the bulbo-spinal group; (*d*) the encephalitic vital centre group. For each of these groups the condition and indications for tracheotomy are discussed. The authors then write about care of the tracheotomy in terms of moisture, suction, supplementary oxygen and clearing of the tracheal tube. Finally, they consider the question of "detubing" the patient.

STEREOPHONIC HEARING. H. L. Hasbin and W. G. Hardy, *Laryngoscope*, October, 1960.

THE authors have investigated binaural hearing aids. They had a reasonable variety of aids which could be loaned to patients on a temporary basis. They divided their patients into five categories. (i) Those with the complicated neural deafness cases; one quarter of these were helped under certain circumstances, whereas all in this group had been unsuccessful with a monaural aid. (ii) Those with mild loss on one side and fairly severe loss on the other; it was found that binaural aids (where the better ear tolerated amplification) helped, especially in complex group situations, for example, board meetings. (iii) Those with moderate to severe bilateral neural deafness; all these patients were benefited with binaural aids. (iv) Those with moderate to severe bilateral, mixed-type impairment; all chose binaural aids. (v) Those with moderate to severe bilateral conductive deafness cases; in general these patients responded well with a monaural aid; some tried binaural aids and enjoyed the stereophonic effect; others tried one instrument and two ear pieces, and also enjoyed the "quasi stereo" effect. The authors discuss the pros and cons of binaural hearing aids. They mention the expense in relationship to result. Careful fitting and mechanical adjustment are important. The use of binaural aids in severely deafened children is also mentioned. There have been some favourable results which, the authors believe, should be investigated further.

Special Article.

LIGHT COAGULATION IN OPHTHALMOLOGY.

LIGHT COAGULATION or photocoagulation has been an exciting recent advance in the treatment of some difficult ocular conditions. An original idea, developed since 1948 by Meyer-Schwickerath in Germany, the light coagulator consists basically of a machine which produces an intense beam of light, at its brightest with an intensity greater than that of sunlight. This beam, focused by ophthalmoscopic control on the fundus, is capable of producing a spot of heat coagulation in the retina and choroid.

The Hospitals Commission of New South Wales has recently installed a light coagulator at the Sydney Eye Hospital, where patients can be referred for treatment. A coagulator is also in operation at the Eye and Ear Hospital in Melbourne. The writer recently had the privilege of attending a course on light coagulation organized by Professor Meyer-Schwickerath at the University Eye Clinic in Essen. The purpose of this communication is to let practitioners know that the machine is available in Sydney, and the conditions for which it is eminently suitable as used in Continental and American clinics and in London, where there is now a coagulator at Moorfields Eye Hospital.

The Light Coagulator.

The idea of therapeutic light coagulation occurred to Meyer-Schwickerath after observing the burn produced at the macula by unwise gazing at the sun's eclipse (eclipse blindness), a condition which is not uncommon in Australia. He thought that if such a burn could be produced therapeutically, it would be a very useful form of treatment for sealing holes in the retina both at the macula and elsewhere.

His first efforts, using sunlight, were successful, but had obvious disadvantages. With the help of the Zeiss Company and considerable experimental work, the present machine was produced. This uses as the source of light a quartz bulb, in which the rare gas xenon is excited to incandescence under pressure by an electric current. Almost the entire energy radiated is in that part of the spectrum to which the eye media are transparent—that is, daylight in the visible region, 3000 to 9000 Å. This beam is directed by an optical system into an ophthalmoscope. While the lesion is being located, a shutter in the ophthalmoscope obscures most of the light beam. On pressing a button on the handle of the ophthalmoscope, this shutter is released, while the examiner's eye continues to be protected, and the full beam is directed accurately into the patient's eye. A wide range of intensities is available, and the size of the focused spot can also be varied for different conditions from 0·5° to 6°.

Principles of Light Coagulation.

Photocoagulation is based on the principle that when an intense light source is focused on the retina, the radiant energy, absorbed by the pigment in the pigment layer of the retina and in the choroid, is transformed into heat. Hence the colour of the tissue to be treated and the degree of pigmentation in the fundus itself are of the utmost importance, more effect being produced in dark than in unpigmented tissue for the same amount of energy delivered.

Cornea, lens and vitreous, being transparent, are unaffected. On the other hand, iris tissue, being pigmented, will absorb considerable amounts of energy, and thus, when fundus lesions are being treated, the iris must be dilated as widely as possible.

Another important factor is the degree of dispersal of local heat production by the very vascular choroid. At one extreme of intensity, no coagulation will occur if the heat produced is not greater than that which the choroidal blood flow can disperse. At the other extreme, an instantaneous dense focus of coagulation occurs before the shutter can be released, with the potential danger of producing an "explosive" reaction in the choroid.

Ideally, the intensity is chosen — and this requires experience — which produces coagulation in about one second. At this point the retina over the focus area turns white, the appearance being very similar to a small patch of acute choroiditis.

Meyer-Schwickerath found in rabbits, after repeated exposures to intense light, that a maximal increase in temperature of 1° C. occurred in the ocular media, and concluded that if exposure was limited to the amount needed for therapeutic coagulation, no danger existed for the ocular media or iris.

Peripheral retinal lesions, which can be reached if necessary by indenting the sclera, require a greater intensity for a given effect than do central lesions. Transparency of the media is also, of course, of importance.

After coagulation and over the next few days, the treated area becomes slightly larger, showing that an effect is produced in the tissue in a concentric zone just beyond that which is immediately visible. Pigmentation begins to appear at the periphery of the lesion in four or five days and at the centre of a large area in two weeks or so.

For children general anæsthesia is, of course, necessary, but adults are treated with retrobulbar anæsthesia.

Therapeutic Uses of the Coagulator.

Retinal Detachment.

The coagulator can be used to close retinal holes or to seal off areas of retinal degeneration which may be potential causes of retinal detachment. However, from the foregoing it will be appreciated that to treat retinal holes the retina must be almost in contact with the choroid. In the presence of subretinal fluid, the coagulation produced in the pigmentary layers would not at the same time involve the retina, and no useful purpose would result. However, a shallow detachment, particularly if the hole is small, may flatten out with binocular bandages and bed rest, and the hole may then be light-coagulated. Also, after routine retinal detachment surgery, if the hole has not been quite closed by the diathermy and the retina is flat enough, it may be sealed by light coagulation; or if there are holes on opposite sides of the globe, the larger may be treated by surgical methods, subretinal fluid drained and the other hole sealed by light coagulation at the same time.

Macular holes are ideally suitable for light coagulation. The question as to whether a lesion at the macula is a hole or a cyst is a vexed one, and factors such as visual acuity and the possibility of detachment occurring need consideration before light coagulation is recommended. However, if central vision has already been lost, it would seem reasonable to seal off the area if any doubt exists.

Equatorial degenerative areas in the retina can be surrounded and sealed off by light coagulation. This should be seriously considered if there is a strong family history of detachment, or if detachment has already occurred in the other eye.

In extreme cases the whole periphery can be treated at several sittings at a few weeks' interval; or another method is to divide the retina into wedge-shaped sections by light coagulation to confine the separated area if detachment occurs.

In Meyer-Schwickerath's series of over 1000 prophylactic light coagulations, about 1% of patients developed detachments after treatment; some of these, he believes, probably occurred in spite of prophylaxis rather than because of it.

Light coagulation also lends itself to the confinement of retinoschisis or stationary peripheral retinal detachment, if interference is thought to be necessary, by coagulation beyond the detached area.

Vascularization.

In Coats's disease and other conditions of neovascularization causing repeated vitreous hæmorrhages, the abnormal vessels can be destroyed.

Angiomatosis retinæ (von Hippel-Lindau) responds well, particularly if the tumours are small. Large masses require several treatments spread over a period, but the method has the great advantage over diathermy that it can be repeated as necessary and localization of the tumour on the scleral surface does not arise.

Choroidal Melanoma.

Since 1952, Meyer-Schwickerath has been treating choroidal melanoma, many of the eyes being enucleated during the course of treatment to study the effect. Of the remainder, the majority have so far been clinically cured. In the present state of our knowledge, one is entitled to have doubts about treating melanoma when the other eye is normal, but if an only eye is involved it could well be justified.

Without going into details of treatment, it is recommended that light coagulation would not be practical if the tumour is too high (more than 6 dioptres), if it extends to the ora serrata or disk, or if there is too much exudative detachment. If special reasons exist, choroidal metastases can be similarly treated.

Retinoblastoma.

As a result of success with choroidal melanoma, retinoblastoma has been similarly treated by Meyer-Schwickerath since 1954. Although the tissue is white, coagulation can be successful, because the light is transmitted to the choroid and the tumour is very sensitive to loss of its blood supply. Small tumours of one disc diameter can be readily destroyed by one coagulation; but large tumours of, say, one-quarter the total retinal surface are difficult to treat with light alone, and for these light coagulation is better combined with other methods.

Probably the most useful application of light in this condition is in the treatment of the other eye, in which the tumour should be discovered while it is still small, during the usual observation period; or of the first eye when a strong family history exists.

Iris Conditions.

A different head can be attached to the coagulator, which allows for the light rays to emerge as a converging beam instead of parallel rays. By focusing this beam on the iris at the required intensity, a coagulation will occur leading to a hole in the iris in two or three weeks. At high intensities, an actual "explosive" effect occurs in the iris with immediate hole formation. The most frequent application of this procedure is, of course, in aphakic eyes when the pupil has been drawn up beyond the visual axis.

There are other iris conditions which lend themselves to light coagulation—for example, tumours, if they are not too close to the pupillary edge (where the lens may be injured) or extending into the angle.

Dangers of Light Coagulation.

Potential danger exists for both operator and patient. The only danger to the operator is if he is careless enough inadvertently to direct the beam into his own eye and produce a macular burn.

In the patient's case, fresh holes may be produced in the retina by the coagulum separating, if an attempt is made to seal off a spreading detachment. Excessive intensity can produce an explosive choroidal reaction and vitreous hæmorrhage.

Attempts to do too much to the fundus at one sitting can lead to destructive uveitis. Similarly, severe iridocyclitis can be produced by excessive coagulation or by using too large a target with an inadequately dilated pupil.

Light coagulation will no doubt become a more important instrument for treatment as we learn to use its full capabilities and at the same time realize its limitations.

EDGAR J. DONALDSON, M.B., B.S., D.O.,
Honorary Staff, Sydney Eye Hospital.

British Medical Association.

NEW SOUTH WALES BRANCH: SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on November 24, 1960, at the Robert H. Todd Assembly Hall, British Medical Association House, 135 Macquarie Street, Sydney, DR. B. A. COOK, the President, in the chair.

The Arthritides (Non-Infective).

DR. E. A. JACKSON read a paper entitled "The Non-Infective Arthritides" (see page 86).

DR. S. G. NELSON read a paper entitled "The Non-Infective Arthritides". This paper has not been made available for publication.

DR. R. G. ROBINSON, in opening the discussion, said that all the syndromes mentioned were inflammatory processes affecting the connective tissue. That inflammation was the consequence of a chemical irritant or irritants, whether endogenous or exogenous, whether direct or indirect, in their effect on the tissues. Control could be obtained with one of the many anti-inflammatory agents available; but present knowledge of the chemical irritants and of all the processes surrounding them was poor indeed.

Dr. Robinson went on to say that in inflammatory joint disease there was, in a broad sense, only one form of clinical pathological process, the inflammation of soft tissues related to the joints, since it was known that degenerative changes of extreme degree might be of little clinical or functional importance. Degenerative disease of joints was a normal function of aging. It amounted to a wearing down of hyaline cartilage. A reflex effort at repair was abortive, and resulted only in increasing inflammation according to the speed and degree of the process and to the amount of trauma to which the joint was subjected. In that way degenerative disease might be replaced by secondary osteoarthritis—osteoarthritis secondary to a known traumatizing factor. Primary osteoarthritis implied an exacerbation of the degenerative process by factors which primarily affected the health not only of the hyaline cartilage of joints, but also of the cartilage of other parts such as the ears, nose and glottis. When trauma acted on that unhealthy cartilage, a state of destruction occurred, producing inflammation beyond the capacity of local resistance. Other elements of the joints became involved, and a painful, sometimes crippling, syndrome resulted. A classical example of that was seen in primary generalized osteoarthritis, in which a group of joints was involved—the terminal interphalangeal joints of the fingers, the first carpo-metacarpal joints, the cervical part of the spine, the lumbar part of the spine, the knees and the first metatarso-phalangeal joints. That condition might be so acute as to cause an erroneous diagnosis of rheumatoid arthritis, particularly if the proximal interphalangeal joints of the fingers were involved (Bouchard's nodes) and the erythrocyte sedimentation rate was elevated.

It was known that inheritance of poor-quality cartilage, mental and physical stress, dehydration, excessive fat intake, deficiency of vitamins A, D and C, allergic phenomena, disease toxins, toxic metabolites, defects of thyroid, adrenal, pituitary and gonadal gland function, tumours and vascular disorders all adversely affected the health of cartilage. A diagnosis of osteoarthritis which did not include the causal mechanism was of little value.

Dr. Robinson finally said that the arthritides in which soft-tissue elements of joints were primarily affected created their own problems during activity. In remission, each in its own peculiar way added to the problem of joint degeneration. Rheumatoid arthritis and ankylosing spondylitis in their many forms and in their multitude of presentations exhibited as a characteristic change joint capsule inflammation. Despite all the available information about their intimate micropathology, they both presented continuous capsular inflammation—different in presentation because of the larger point in tissue microchemistry, whether genetically or environmentally determined. The onset and progress of the disease might again be related to, if not associated with, many factors. In some cases the relationship with infection (as in Reiter's disease) seemed to be of great importance. Autosensitization or hypersensitivity phenomena were adduced to explain the persistence of the disease.

Dr. Nelson, in reply to Dr. Robinson's comment on the importance of the microchemistry of collagen tissue, said

that he thought the trend at the present time was a little away from the collagen tissue itself. Much time and effort had been put into the study of the microchemistry, and into the electron microscopy and other minute study of the collagen tissue. It had not been rewarding—not much abnormality could be demonstrated in it. The adsorption of plasma proteins and the presence of all the active cells in collagen tissue showed it to be acting as a kind of scaffold for what was occurring on it. With regard to what had been said about the factors controlling the health of the tissues in collagen diseases, Dr. Nelson said that he agreed entirely.

In reply to Dr. Wing, who had deplored the fact that patients depicted in the slides had been seen only in the late stages, Dr. Nelson said that it was regrettable that in standard textbooks the more dramatic and late forms of the disease were those selected for illustration. It was possible that they had fallen into the same trap. In point of fact, the disease was one which had a commencing point; one of the hardest things in clinical practice was to make the diagnosis early with little clinical, radiological or pathological evidence to go on. That applied to the whole range of those diseases. The more they understood about the natural history of the disease, the better they would be at picking the diagnosis early.

DR. A. KITCHENER SMITH commented on the fact that the diseases under discussion were being more and more divided into separate entities. When they were observed from the other end of the telescope, the similarities were seen. Dr. Kitchener Smith asked Dr. Nelson to comment on the fact that the nodules in juvenile rheumatoid arthritis were more characteristic of rheumatic fever than of adult rheumatoid arthritis. Dr. Kitchener Smith also asked Dr. Nelson to make some mention of serology and to comment on the protein picture in rheumatoid arthritis; he understood that it was one of the most characteristic signs.

Dr. Nelson, in reply, said that he required notice of the second question. It was difficult to give a picture of the protein changes. It was known that the rheumatoid factor was one of the things found constantly; but there were a number of other changes in the electrolyte pattern. Investigations by the ultracentrifuge method had identified the rheumatoid factor as lying in two planes. With regard to the similarity of the nodules, Dr. Nelson said that the fact was tied up with the rather unimaginative types of reaction of connective tissues that he had mentioned. There was a very close similarity between rheumatoid arthritis and rheumatic fever; the first simply looked a little more grown-up and mature. That illustrated a number of other features; changes similar to polyarteritis nodosa might be seen in rheumatoid arthritis, those in scleroderma might be seen in lupus. It was the overall picture rather than the detail that made the diagnosis.

The question was asked whether the speakers had had any experience of ankylosing spondylitis in female patients. He said that he believed it had been recorded with a different radiological picture.

Dr. Jackson, in reply, said that he knew only the clinical ratio, which was 9·5 to 10 to 1. He had seen only a few cases of ankylosing spondylitis over the last few years, but could not recall seeing it in a woman.

DR. R. W. THOMPSON said that rheumatoid arthritis was a progressive disease, and as Dr. Wing had said, before gross distortion occurred, there were certain clinical measuring rods of severity. Dr. Thompson asked Dr. Nelson what he thought of commencement in, for example, the synovial membrane. Was it a *sine qua non* of commencing rheumatoid arthritis of the capsule?

Dr. Nelson, in reply, said that it was impossible to see the earliest changes unless one examined a biopsy specimen. It appeared that pathologists now agreed that the very earliest change was in the synovial membrane. In certain rather explosive situations one might find similar pathological changes in the other place. As Dr. Kitchener Smith had pointed out, very early in the disease a change was found in the plasma proteins. The question was, which came first? The majority of patients presented themselves at a stage when they would have recognized changes in the synovium. However, what one saw on clinical examination was a patient with an inflamed joint, limited movement, morning stiffness, etc. One had to go on the sum of all the clinical facets of the disease.

Dr. Cook asked what was the present position of certain highly vaunted drugs in the treatment of the diseases. Had vaccine therapy any place? Was gold in the discard?

Dr. Nelson, in reply, said that he could not cover treatment in the twenty minutes allotted for his paper. The thing that had emerged from the more recent studies was the immense value of the basic treatment programme—rest, splinting of actively inflamed joints, the use of rather simple analgesic and anti-inflammatory drugs, and the general management of the patient. That was best exemplified in Britain in Duffy's clinic, where patients in the early stage could be admitted and have treatment. In the U.S.A. the question of cost loomed large and influenced treatment, but it was possible to get it. Simple aspirin and salicylate treatment had much merit. The state of the patient three, four or five years after the commencement of the disease was much better if a basic programme of elimination of strain on the joint, rest, aspirin, etc., was followed. A therapeutic trial indicated that there was a significant difference between patients who received gold in accepted dosage and those who received a token dose to serve as controls. However, those who went into remission did have progressive distortion of joints; gold was not the complete answer. "Butazolidin" was a very good analgesic agent; the evidence that it had any antirheumatic or anti-inflammatory power was much less definite. In his practice the dosage was gauged very carefully; the loading dose was 600 mg., and the maintenance dose 200 mg. There were no toxic effects, provided suitable patients were chosen. Gold and "Butazolidin" should not be mixed; both were toxic to the bone marrow. There was some optimism that chloroquine and other synthetic antimalarials would assist in the production of a clinical remission in a proportion of cases. However, chloroquine had certain hazards too; it was necessary to watch for depositions in the eye, and for curious changes in the colour of the hair. The dose was 150 to 300 mg. per day, and it could be continued for some time. Some patients did not tolerate it. Referring to the steroids, Dr. Nelson said that the more he saw of the results of treatment with those agents, the less anxious he was to use them. It was delightful to see patients get better on the initial dose, but there were many disappointments. The mortality rate was much higher among patients receiving maintenance steroid therapy than among patients not on steroids. The hazards were many — intercurrent infections, unrecognized ulcers, etc. Steroids were given to patients who otherwise would be wheel-chair cripples; steroids had a place in the treatment of rheumatoid arthritis only after other measures had been tried and after careful consideration of the risks.

Dr. Cook, from the chair, said that those present had had an interesting evening's discusion of a disease that was disappointing to patient and clinician. An excellent survey had been given by both speakers.

Out of the Past.

THE DOCTOR'S HOLIDAY.[1]

[To the Editor of the *Australasian Medical Gazette*, February 20, 1903.]

SIR,—The temporary exchange of practices suggested in an Editorial of your last issue might do for a man whose exchequer won't stand a *locum*; but the ideal holiday is an anchorage to some part of this earth, a long, long distance from the grumblings of the chronic and the plaintive appeals of the infant engaged in the throes of teething—a long way off, in fact, from the depressing effects of the sombre-visaged hypochondriac and the maunderings of the household Martha, which act like a sinapism on the over-worked club doctor.

In an exchange of practices there would be no escape from the lamentations of the hollow-cheeked female with that everlasting backache; whilst the medical gentleman with a brand new theory on something-or-other, and an up-to-date method of treating it, would still clog our weary steps and make our lives (or holiday) an uninterrupted torment.

Give this humble scribe a tent, a billy and some hash, and a week in a mountain fastness of this great country, with the twinkling of stars and a scalper chop for companions, and his lullaby the weird, soul-stirring sound of the marauding dingo, and he doesn't want anything else until that week is up—unless it's another week of the same sample! I am, sir, etc.,

Newcastle. R.H.T.

[1] From the original in the Mitchell Library, Sydney.

Correspondence.

AN AUSTRALIAN MEDICAL ASSOCIATION.

SIR: We should thank Sir Henry Newland (MED. J. AUST., June 10, 1961), for exposing the main weakness in this proposed constitution. He has sufficient experience and wisdom in medico-political matters to see the grave danger, which, in spite of all Dr. Colville has said about constitutional means and democratic ideals, appears to have been missed. There is nothing in the Australian Medical Association constitution to safeguard the 11,000 doctors from civil conscription if the Labour Party were to repeal the *National Health Act*. Sir Henry is absolutely right in his suggestion that the referendum should be held, and it is a simple matter to print 11,000 relevant circulars appropriately worded, perhaps like this: "Before acceptance should provision be included in the constitution to protect doctors against civil conscription and to preserve freedom of choice—Yes or No."

Certainly a mandate has been given for steps taken by the Federal Council; but the steps not taken are far more important, and it has been left to Sir Henry Newland to indicate the fault which should have been seen by the Steering Committee originally. The average doctor is now far more aware of the danger of civil conscription than he was twelve months ago, and no effort on the part of the Federal Council should be spared to ensure that his interests are adequately protected, even though it may delay final acceptance of the constitution.

The fact that responses to previous referenda have been poor merely shows how badly organized we are. It is only in the last twelve months that Victoria has introduced a workable system for obtaining rapidly opinions of members on various potent issues. The whole matter should be delayed further until all rank and file members have been consulted. Too much emphasis is being placed on launching the new association in January, 1962. Failure to do this will not cause half the financial concern that would result from too rapid acceptance of a constitution which fails to protect us from a hostile government.

Talk of provision being included later for modification does not impress me; nor did it satisfy country representatives at the recent Convocation in Melbourne, where fears were expressed that the profession was being asked to accept a constitution in which inadequate provisions existed for reasonably speedy modification. Dr. Colville asks that members support the Federal Council rather than criticize it, but fails to appreciate the serious omission so clearly expressed by Sir Henry. Many of us are uneasy about the whole thing, and the Federal Council deserves to be criticized for overlooking a golden opportunity to unite the profession openly against our greatest enemy, "civil conscription"—in other words, "nationalization by statute". A referendum is the only really effective way of doing this, and if the Federal Council has any organizing ability at all, six months should be plenty of time in which to see it through. Perhaps the referendum could be carried further and used to sort out those who are really against nationalized medicine from those who appear lukewarm. Unity cannot possibly exist while these facts are unknown.

Yours, etc.,

17 Scoresby Street,
Kerang,
Victoria.
June 16, 1961.

HUGH T. MCDONALD.

CONGENITAL MALFORMATIONS AND MATERNAL RUBELLA: PROGRESS REPORT.

SIR: To the mind of this ophthalmologist, the ocular prognosis in David B. Pitt's paper on the above subject (MED. J. AUST., June 17, 1961) smacks of undue optimism. On page 888 he says "minor defects such as rubella retinopathy have been omitted", but I have seen patients with this condition in whom the central vision has been considerably impaired. On page 889 he states that only two severe eye defects have been recorded in his series, both of which were unilateral. Yet Table X mentions two cases of left cataract, one of left hydrophthalmia and one of cataracts with microphthalmia. In Table X his statements, or lack of them, in the "Remarks" column about Cases 54, 131, 163 and 170 look strange when compared with the diagnosis. It is to be hoped that his final report, which should be accompanied by a more detailed description of both the ophthalmic findings and their treatment, will be delayed long enough to include an accurate assessment of each living child's vision by means of the Snellen chart. Dr. Pitt realizes that some of his observations cannot be properly assessed for at least another two years; but it would be unfortunate if his present preliminary report should mislead any readers as to the probable seriousness of the visual defects in these embryopaths.

Yours, etc.,

104 Brougham Place,
North Adelaide.
June 22, 1961.

D. O. CROMPTON.

"TES-TAPE" AND "URITAPE".

SIR: These two preparations for the measurement of glucose in urine have recently been placed on the list of Pharmaceutical Benefits. "Tes-Tape" is an indicator paper containing glucose oxidase, peroxidase and *o*-tolidine (Seltzer and Loveall, 1958). "Uritape" also is an indicator paper containing, we believe, a similar system.

In the past, there have been several reports (Hunt, Gray and Thorogood;[1] Tunbridge, Paley and Coulson;[2] Leonards,[3] Jablokow, Hutchins and Knights[4]) that "Tes-Tape" tends to under-estimate glucose in urine when present in concentrations over 0·5%. On the other hand, Seltzer and Loveall[5] have claimed that "Tes-Tape" is reliable at all glucose concentrations if it is used in a particular manner now recommended by the manufacturer.

In view of these conflicting reports and because we were unable to find any report on the reliability of "Uritape", we have reexamined the use of such tests for the semi-quantitative measurement of glucose in urine, comparing the results with those obtained by a quantitative method measuring true glucose and with those obtained with a copper-reduction method—namely, "Clinitest".

TABLE I.

Comparison of Results Given by "Uritape" with True Glucose Concentration.

True Glucose. (Grammes per 100 ml.)	Number of Urines.	Distribution of Urines According to the Results Given by "Uritape".				
		0%.	0·25%.	0·5%.	1%.	2% or Over.
<0·18	31	**24**	7			
0·25[1]	6	1	**5**			
0·5[1]	12		1	**7**	4	
1·0[1]	14		1	5	**8**	
>1·50	37			5	18	**14**

[1] The limits of groups were: 0·25, 0·18–0·37; 0·5, 0·38–0·74 1·0, 0·75–1·49.

The urines were some of those brought by non-pregnant patients to the diabetic out-patient clinic of St. Vincent's Hospital, Melbourne. Each urine was examined without delay according to the instructions laid down by the manufacturer by one operator using (*a*) "Uritape", (*b*) "Tes-Tape" and (*c*) "Clinitest". The manufacturers of "Uritape" state that the colour given should normally be read at 30 sec., but, if reactions are consistently slow, readings should be made at 1 min. instead of 30 sec. In this survey, "Uritape" was read at 30 sec. in every instance, since we felt that it was impossible to decide in a particular urine whether the reaction was slow or not. The true glucose content of each urine was then determined quantitatively by another operator using a glucose oxidase method (Watson)[6].

The results are given in Tables I to III. Urines were grouped according to the true glucose concentration. The

[1] *Brit. med. J.*, 1956, 2: 586.
[2] *Diabetes*, 1957, 6: 426.
[3] *J. Amer. med. Ass.*, 1957, 163: 260.
[4] *J Amer. med. Ass.*, 1958, 167: 1826.
[5] *Brit. med. J.*, 1956, 2: 588.
[6] In the press.

results of the semi-quantitative tests are expressed as the number of urines within each group giving a particular result with the test in question. Figures in the diagonal column (bold type) represent urines in which there was satisfactory agreement between true glucose values and the result of the semi-quantitative test. Figures falling outside the diagonal column represent urines in which the semi-quantitative test gave an error of more than 33%.

It is clear from Tables I and II that both "Tes-Tape" and "Uritape" gave misleading results in a relatively large proportion of urines. In particular, both tests frequently under-estimated the concentration of glucose present when this was large. In addition, with "Uritape" some urines

TABLE II.

Comparison of Results given by "Tes-Tape" with True Glucose Concentration.

True Glucose. (Grammes per 100 ml.)	Number of Urines.	Distribution of Urines According to the Results given by "Tes-Tape".				
		0% or 0·1%.	0·25%.	0·5%.	—[1]	2% or Over.
<0·18	14	**14**				
0·25[2]	4		**4**			
0·5[2]	7		3	**4**		
1·0[2]	7		2	5		
>1·50	31		6	21		**4**

[1] "—" = The "Tes-Tape" colour chart does not give a 1% reading.

[2] See footnote, Table I.

containing very little glucose were recorded as having 0·25% glucose. This was not so with "Tes-Tape", though it should be pointed out that urines giving a slight reaction (0·1%) with "Tes-Tape" were tabulated with those giving no reaction, whereas with "Uritape" such urines were recorded as having 0·25% glucose, the lowest positive value recordable with the colour chart supplied.

TABLE III.

Comparison of Results Given by "Clinitest" with True Glucose Concentration.

True Glucose. (Grammes per 100 ml.)	Number of Urines.	Distribution of Urines According to the Results Given by "Clinitest".				
		0%.	0·25%.	0·5%.	0·75% or 1%.	2% or Over.
<0·18	31	**31**				
0·25[1]	6	1	**5**			
0·5[1]	12			**11**	1	
1·0[1]	14			2	**12**	
>1·50	37				7	**30**

[1] See footnote, Table I.

The reason for these discrepancies is not altogether clear. However, when urines were diluted before testing, both "Uritape" and "Tes-Tape" gave results (allowing for dilution) much more in agreement with the true glucose content. This suggests that the concentration of certain urinary constituents present in undiluted urine interferes with the reaction. Dilution of the urines, as is employed in the true glucose method, abolishes this interference. At low glucose concentration—that is, below 0·18 gramme per 100 ml.—"Uritape" appears to be too sensitive.

In contrast, the results obtained with the copper-reduction method ("Clinitest") were very much more in agreement with the true glucose values (Table III). Discrepancies occurred mainly with urines containing more than 1·5 grammes per 100 ml. glucose. Of the seven urines in this group giving low values with "Clinitest", three contained only just more than 1·5 grammes per 100 ml. glucose (namely, 1·50, 1·50 and 1·60 grammes per 100 ml.). The other four urines in this group giving low results contained more than 2 grammes per 100 ml. glucose. In urines with more than 2% glucose, the final colour—namely, greenish-brown—is similar to that given by urine containing about 1% glucose, though the reaction mixture turns orange at one stage. Occasionally, this sequence of colour changes is not readily detected, so that urine actually containing more than 2% glucose appears to contain only 1%. However, such an occurrence is infrequent and the resulting error relatively unimportant.

Yours, etc.,

I. J. HOPKINS,
J. A. OWEN,
Biochemistry Laboratory, St. Vincent's Hospital.

D. WATSON,
Biochemistry Laboratory, Royal Women's Hospital.

Melbourne.
June 16, 1961.

THE PATIENT HAS RIGHTS.

SIR: In the ever-increasing post-graduate and student clinical sessions and seminars in modern hospital life, it is not out of place to remind those presenting and discussing cases that the patient is human and usually very interested in his or her condition. At unguarded moments it is possible for remarks to be picked up, especially concerning prognosis, which cause considerable distress. Our old chiefs taught us kindliness and humility. One hears and knows of too many instances of patients being regarded as material rather than personalities.

A glaring instance occurred recently, when the prognosis of a patient in a large non-teaching metropolitan hospital was openly discussed, leading to severe and persisting mental stress.

Patient care must always come first in our hospitals before educational and research items.

Yours, etc.,

ERIC GOULSTON.

B.M.A. House,
135 Macquarie Street,
Sydney.
June 20, 1961.

MENTAL HEALTH CONFERENCE.

SIR: In Canterbury (New Zealand), a mental health council has been formed with the aims and objects of raising the level of knowledge among all sections of the community about the facts of mental health and disease, encouraging research into mental health and disease, and assisting in every way individuals and agencies, voluntary and governmental, already working in these fields. The constitution of the Canterbury Mental Health Council is probably unique. Below are some of the organizations to which members of the council belong: the professions of medicine, nursing, the ministry, law, accountancy, and teaching; Canterbury University Council and staff; junior and senior chambers of commerce and the Canterbury Manufacturers' Association; the National Council of Women; the Plunket Society; the Rotary and the Lions Clubs; the Public Service Commission; the trade unions; the Health Department; the Mental Health Association; the City Council; the New Zealand Broadcasting Service; and the Returned Services Association. The Council was organized early in 1960 and, shortly thereafter, was incorporated under the *Charitable Trust Act*. After Council members had considered the ways in which they could begin work for mental health in Christchurch, they decided the first project should be in the form of a community-wide educational programme.

Last year, the students of Canterbury University collected £4000 on "Procesh Day" and donated the entire proceeds to the Mental Health Council. Further financial assistance has been offered by Smith, Kline and French, Pfizer, Roche and Geigy pharmaceutical firms. This financial support has made it possible to plan a major mental health conference in recognition of World Mental Health Year. Seven distinguished visitors have been invited from outside the country, and many New Zealanders will participate formally.

The programme will last two weeks in August-September, 1961. The first week will be devoted to professional groups, the second to the lay public. It is felt that non-medical professional groups, such as clergy, lawyers, nurses and school teachers, as well as medical practitioners, psycholo-

gists and social workers, should participate together in the first week's learning experience, since all have vast social responsibilities in their daily work. There will be meetings restricted to medical practitioners. However, it is also thought desirable to have combined meetings at which doctors will sit with members of other professions whose work brings them into daily contact with people needing professional help for emotional or mental disability. If we are to work towards the prevention of emotional disorder, it is necessary that each of the various groups should understand the roles and attitudes of the others and learn to work harmoniously with mutual respect and in close cooperation.

Since Christchurch is now only a few hours' flight from Sydney and Melbourne, it is hoped that a number of "Aussies" will attend the conference. Visiting doctors' wives interested in the programme would be welcome to register and attend the general sessions.

Yours, etc.,

DAVID LIVINGSTONE,
Chairman, Professional Education Committee, Canterbury Mental Health Council.

110 Park Terrace,
Christchurch,
New Zealand.
June 21, 1961.

EXTERIOR GESTATION AND LIFE SET.

SIR: Lest any readers should fall into the slough of despond through reading the letter by C. G. Judge on "Exterior Gestation and Life Set" in your issue of June 24, may we be permitted a brief comment?

Far from ushering in an era of psychiatric gloom, the concept of exterior gestation suggests a hopeful approach to many medical and psychological problems. Not the least involve the staggering increase of psychosomatic and behavioural disorders here and overseas. If by delineating an evolutionary approach to the problems of infancy a new area for research in prophylaxis has been revealed, surely the prospect spells the antithesis of despair, since it is universally conceded that prevention is better than cure. Even if such an approach merely led us to understand the techniques whereby the Australian aborigines are almost free from allergies, it could lead to a therapeutic triumph. Far more than this seems possible.

Yours, etc.,

JOHN BOSTOCK,
MARJORIE SHACKLETON.

Department of Medical Psychology,
University of Queensland,
Brisbane.
June 28, 1961.

TRIBULATIONS OF A DOCTOR'S WIFE.

SIR: I write this letter more in sorrow than in anger, although I cannot deny that my disappointment is tinged with some resentment.

From my youth I have had foot trouble, some of which was congenital; but most of it has been acquired, partly through stress and strain, and partly through surgical interference.

1. My first operation was a success; it consisted of the elevation of a skin flap, bearing a corn, from the surface of an exostosis (on the first metatarsal), removal of the exostosis and replacement of the flap. As the surgeon predicted, the corn soon disappeared and I gained relief.

2. After the death of my first surgeon, I consulted surgeon II, who did the same operation on the other big toe (right). But this time the wound suppurated, and healing took place with much scarring and resultant stiffness.

3. This time I had Keller's operation done on both big toes. That on the left side proved satisfactory, with good movement, but the right big toe remained stiff and overextended. The right foot became progressively worse, plantar corns formed from maldistribution of pressure and weight-bearing became more and more painful.

4. My fourth surgeon was asked if he could improve the position and movement of the right big toe. He placed a piece of fascia lata in the old joint space and also removed the base of the first phalanx of the second toe, because it was projecting too far beyond the other toes. This left the foot weaker, and a new series of corns developed. The big toe was no better, but I was prepared for this by the surgeon's preliminary warning.

5. The most painful area was under the head of the third metatarsal when I consulted the next surgeon. He removed the head of the *second* metatarsal and cut the extensor tendons of the four outer toes, none of which were causing any trouble; they have remained weak, with permanent loss of extension. Weight-bearing became more painful now, and I had to make do with pads and props. He did, however, straighten the big toe with benefit.

6. A year or two later a monograph, "Surgery of the Foot", was published in America. Personal correspondence between the author and my husband gave hope that here might be found salvation. For some time we had thought that repair was needed—replacements, not removals—and this surgeon agreed. This meant an expensive and inconvenient trip to the States, but the result has justified it. I now quote from the clinical notes:

> Diagnosis: Intractable plantar keratosis under the third metatarsal head of the right foot, secondary to surgical absence of the head of the first and second metatarsals and half of the proximal phalanx of each of these toes.
>
> Operation Findings: There is a deep seated keratotic lesion under the third metatarsal head. Part of the head of the second metatarsal is absent as is the head of the first metatarsal. The base of the proximal phalanx of the hallux is absent and about three-fourths of the shaft of the proximal portion of the first phalanx of the second digit is also absent.
>
> The operation: Plantar condylectomy (of third metatarsal head) and fibular graft to the second metatarsal shaft.

The graft is described as a "step-down" type, and it was fixed to the metatarsal shaft with three strands of fine wire.

The foot is still far from perfect, but I can stand and walk with relative comfort; the stiffness of the big toe and loss of extension of the outer toes still handicap me.

All the anæsthetics, some local, some general, were successful.

Yours, etc.,

June 3, 1961. "SIM".

THE PROBLEM OF VENEREAL DISEASE.

SIR: Figures quoted recently in this Journal (January 21, 1961, page 111) showed an increase in the incidence of syphilis reported in Australia, from 459 cases in 1954 to 664 cases in 1959; patients with gonorrhœa increased from 1944 cases in 1954 to 4128 cases in 1959. These figures are somewhat similar to those reported in Britain (Nicol,[1] British Ministry of Health,[2] Mascall[3]), new cases of gonorrhœa reported from venereal disease clinics in England and Wales having risen from 18,064 in 1951 to 31,344 in 1959, and although the number of cases of syphilis reported has fallen from 8432 in 1951 to 3927 in 1959, there has been of late an increase in the number of recently infected new cases from 704 in 1958 to 773 in 1959. Nicol, commenting on the apparent decline in the overall number of cases of syphilis treated at venereal disease clinics, states: "It should be clearly understood that the Ministry of Health returns do not indicate the true prevalence of venereal disease in this country, as cases diagnosed by general practitioners or consultants in private practice are not included." Later he says: "It is possible that this decrease is partly accounted for by the suppression of the early signs of the disease by the widespread use of antibiotics which have some therapeutic effect on syphilis. These drugs are often used symptomatically, thus preventing a diagnosis being made. If they are not given in adequate dosage they will not cure early syphilis, which becomes latent and may in due course give rise to clinical late syphilis." Of some interest in this regard is the report of Bockner and Coltart[4] regarding an increase in the number of cases of general paralysis of the insane admitted to their hospital from an annual average of one or two to nine cases in 1959.

[1] *Brit. med. J.*, 1961, 1: 445.
[2] British Ministry of Health (1960), Report for the Year 1959, Part II, H.M.S.O., London.
[3] *Brit. med. J.*, 1961, 1: 899.
[4] *Brit med. J.*, 1961, 1: 18.

At the Royal Newcastle Hospital the number of cases of primary syphilis diagnosed at the male venereal diseases clinic each year from 1956 to 1960 (inclusive) has been 8, 4, 7, 5, 9, and new cases of gonorrhœa during the same period have been 65, 75, 67, 78, 137. To date this year, 16 cases of primary syphilis have been diagnosed (mostly by dark-ground illumination) and 60 new cases of gonorrhœa, and although chance distribution could account for this increase to some extent, it seems probable that the figures reflect the increase reported elsewhere. It would certainly be interesting to know the true incidence of syphilis and gonorrhœa in the community; that it is greater than the statistics of reported cases would indicate seems quite likely, for reasons given by Nicol.

It is of interest that some of these new cases of syphilis were blood donors, and although dark-ground examination of fluid from the chancre in each case showed numerous spirochætes, serological tests for syphilis, as might have been expected, were negative. The fact warrants further thought.

Yours, etc.,

W. F. HUNTER,

The Royal Newcastle Hospital,
Newcastle,
New South Wales.
May 10, 1961.

Obituary.

ROBERTA HENRIETTA MARGUERETTA JULL.

WE are indebted to DR. BERTRAM C. COHEN for the following account of the career of the late Dr. Roberta Jull.

On March 6, 1961, the grand old lady of Western Australian medical practice died at the age of 89. Her life was brimful of ceaseless work and unselfish service. She was born in Glasgow, where her father, Dr. Robert Stewart, a Presbyterian minister, had gone on a temporary exchange of pulpits. The family returned shortly after to Portugal, and her early childhood was spent in Lisbon.

Her mother, *née* Fergusson, whose name the family still retain, died in Glasgow in 1890 at a comparatively young age. Her father was an extremely learned man, and after retirement from his 30 years' church work in Lisbon he spent considerable time re-translating the Bible from the original Hebrew and Greek. On one occasion he was visited by Arabian missionaries who came to Lisbon. They carried on conversation in the only language common to them all, which was Latin. He died at the age of 76, and was buried at the Stewart's place at Renfrew. It was because of the old man's failing condition that Roberta eventually decided to come out to Western Australia to join her brothers.

Even from childhood Roberta had intended to study medicine, perhaps influenced by her elder brother Mitchell, who had gone to Glasgow for that purpose. She recalled how she helped to dissect the animals on her grandfather's farm and to perform first aid on the other girls at school. She finally nursed both her mother and father in their last illnesses. In 1890, when she was aged 18, she began her first year at the Glasgow University in Queen Margaret College, under very great difficulties because of the prejudice against women doctors. The older professors refused to lecture to them and they had to rely on the goodwill of younger lecturers. There were no mixed classes, and the women had to attend separate lectures and separate hospitals. This entailed a terrific amount of travelling to the various hospitals in different parts of Glasgow. Roberta wisely took an extra year for her course so that she would not break down. This proved a good investment, for in the extra year she was able to do special work in ophthalmology and obtain a resident post at the Eye Infirmary. This was an achievement, because she was the first woman doctor to obtain such an appointment. She obtained her degrees of M.B., Ch.M. in 1895, and decided to come to Western Australia to join her brothers, who were already in practice here. James Mitchell Young Stewart and J. E. Fergusson Stewart had been very bright students. They both qualified before they reached the age of 21, and had to wait until coming of age before degrees could be conferred on them.

In 1896 Roberta landed at Albany, and soon became aware of the lack of amenities. She told how horrified she was when, having been shown her bed in Albany, she ventured to question the doubtful cleanliness of the bedclothes. The housemaid assured her that the bed had been slept in only one night before her arrival.

The streets of Guildford were very rough and practically unlit, so that it was necessary to carry a lantern. Free passes were available to doctors, but only on goods trains, so Roberta made most of her calls on foot, cycle or horseback. On one occasion she was nearly thrown when her horse shied at a camel, one of the last in Guildford. She and her two brothers divided up the practice; Mitchell stayed at Guildford at the Residency next to the Police Station, Fergusson looked after Millar's Camp at Chittering and Roberta took the area as far as Lion Mill. On one occasion she drove the horse and buggy down to Perth to get antitoxin from Dr. Tratman, who had the only supply. The patient survived the immediate infection, but subsequently died of myocarditis. After a year in the Guildford district, Roberta came to Perth to start her own practice. She was well received by the other doctors, and she quickly built up a large connexion mainly attending to women and children. She was the first woman doctor to practise in the metropolitan area. The first in Western Australia was Amelia Margaret Corliss, M.D., C.M.L.C.P.S. (Ontario, 1885), who practised at Menzies.

In 1898 Roberta married Mr. Martin Jull, Under-Secretary for Works, afterwards Public Service Commissioner. He was an intimate friend of her brother Mitchell. The reregistration of Roberta Jull appears in the Medical Register of 1898. In that same year she and Dr. Horrocks called a meeting of doctors practising around Perth for the purpose of forming a local branch of the British Medical Association. Thirteen doctors attended, and Dr. Jull was offered, but declined, the position of secretary. However, she had the satisfaction of seeing the Branch formed on April 7, 1899, and she took an active part in Branch activities for the remainder of her life. For her work she was made an honorary life member of the British Medical Association in 1930.

She attended various inaugural historic events. At the Menzies Railway opening she met Dr. Corliss. At the opening of the Mundaring Weir Reservoir she and Mrs. C. Y. O'Connor marked the second pipe. She was aboard the first large passenger ship *Prince Regent Luitpold* to enter the new harbour at Fremantle.

Mr. Jull died in 1917, and Roberta resumed medical practice, which she had more or less relinquished. She was appointed the State's first medical officer of schools. In 1920 she was sent by the Government to New Zealand to investigate Truby King's methods and this led to the establishment of the Infant Health organization in this State in 1923-1924. In her first year as School Medical Officer she inspected 3781 children, and in 1924 she inspected 5398. In 1924 there were three Infant Health clinics in the metropolitan area. She handed over to Dr. Stang in 1928 the makings of a complete service.

After 1928, Roberta Jull devoted her time to women's organizations and University work. She was president of the National Council of Women from 1930 to 1932, and she was the only woman delegate from Australia to the Tenth Assembly of the League of Nations at Geneva in 1929. Here, at the fifth Humanitarian Commission, she read a paper on "Traffic in Women and Children". At this assembly she was lucky to meet Lady Aberdeen, who entertained her subsequently at her home at Cromagh, from where Roberta was able to check all the family records at Tarland. She took an active part in affairs of the University of Western Australia. She was a member of the Senate for nearly 30 years. She was Warden of Convocation for five years and the Senate representative on the Undergraduate Guild Council. In 1951 the University conferred on her an honorary degree in law. For many years she was president of the Western Australian Association of University Women Graduates. In 1928 she started a committee to raise funds for building a women's college. She was president of this committee until 1945. It took a long time to be finished, so long that ill health prevented Dr. Jull from actually attending the opening ceremony. St. Catherine's is a fitting memorial to her early interest and work in this direction. She was also interested in the teaching of first aid, and for her work she was admitted as a Serving Sister in the Order of St. John of Jerusalem.

Roberta Jull had an indefatigable brain, and her interests were protean. Right up to the end, handicapped as she was by frailty and deafness, she would avidly read medical journals and would carry on conversations and discuss world topics using her antiquated ear trumpet. Her intellect remained bright and her memory keen. She leaves a

worthy representative in her daughter, Mrs. Henrietta Drake-Brockman, one of Australia's leading historical writers. She is remembered with admiration, respect and gratitude.

To fill the hour—that is happiness.

MARSHALL ANDREW.

WE are indebted to DR. G. T. FERRIS for the following account of the career of the late Dr. Marshall Andrew.

Marshall Andrew's many friends were shocked to hear of his sudden death on July 25, 1960, at Newport, Monmouthshire, where he had been staying for several days with a friend, Dr. Brand. He had retired only a matter of months previously from the position of Director of Tuberculosis for New South Wales, which position he had filled with distinction since 1949.

Marshall Andrew was born at Wahroonga, New South Wales, in 1897 and was educated at nearby Barker College and later at the University of Sydney, where he graduated in medicine in 1922, and after a residency at Sydney Hospital, he entered general practice at Picton, N.S.W. It was here, as visiting medical officer to the Queen Victoria Sanatorium, Thirlmere, that he first became interested in tuberculosis. In 1939 he disposed of his practice and went overseas for post-graduate study in his chosen branch of medicine. On his return he was appointed medical superintendent of Bodington Red Cross Sanatorium, which position he held for seven years, when he resigned to commence private practice in his specialty. After a couple of years' successful conduct of this, he was appointed as Director of Tuberculosis of N.S.W. This was at the time when the Commonwealth-sponsored campaign against tuberculosis was about to be launched. The success of this campaign is now history and a lasting memorial to the enthusiasm, drive, and organizing ability of Marshall Andrew. In his friendly way he fitted easily into the Government service, and soon had all his staff fired with his own enthusiasm. With his complete integrity of purpose and sense of fairness, combined with his kindliness but firmness withal, he was the perfect arbiter on tuberculosis allowances. He had, too, the patience and regard for detail for a difficult job. I recollect, at Bodington, in the early days of tomography, that he built his own apparatus from bits of junk, and produced with infinite care and patience some series of films comparable with those from today's modern apparatus.

Away from medicine, Marshall Andrew was quite a sporting personality, with cupboards full of golf trophies from Killara and Leura clubs. He was an avid reader and played a fine game of contract bridge, whilst in photography, both still and movie, he was almost in the professional class. Vintage cars were another hobby of himself and his son John. When between them they owned a fleet of some half a dozen he swore off any addition, but a week later confessed sheepishly to his friends that he had acquired a "glorious old Daimler"—"just couldn't resist the poor battered old thing".

At a large and representative farewell gathering at the Department of Public Health, he was presented with a tape-recorder which was a great joy to him; it took pride of place in his luggage when he flew overseas for the last time. Today in the Tuberculosis Division of the Department there is a quite unusually close and happy liaison with private members of our profession, and one must attribute this happy state of affairs in great measure to the foundation of goodwill laid by Marshall Andrew.

Marshall had never quite recovered from the sudden death of his wife, Nancy, only some eight months before his own. In spite of all his hobbies and interests and his work as an active director in the family printing firm of John Andrew and Co., he appeared restless until he happily resumed part-time work in the Tuberculosis Division reading X-ray films, which work he intended to resume after the last well-earned but ill-fated holiday overseas.

He is survived by two fine sons, John, who is with the family printing firm, and Tony, who is in his final year of medicine.

DR. NICHOLAS LARKINS writes: Marshall Andrew's death is a great loss to the medical profession generally and to sufferers from tuberculosis in particular. To the study of this malady he was dedicated. His appointment as Director of Tuberculosis for New South Wales was a particularly happy one, for in this office he was able to put into effect many of the ideas that had so often occupied his mind in the control of this devastating disease. In this rôle he had an increased contact with members of the profession and the general public. His capacity as a speaker was suited to the rôle of "selling" the campaign against tuberculosis. With his pleasant, charming manner, his whimsical sense of humour and his absolute conviction of what he said, he at once made friends and won the confidence of any audience.

Andrew, in spite of these characteristics, was no "limelight" seeker. He was very popular in Leura, where he lived for many years, was an outstanding golfer and was captain of the Leura Golf Club for a long period. I had the good fortune to know him personally, as did most practitioners in the Blue Mountains area. He supported most loyally any activity of the Blue Mountains Medical Association.

To his family he was devoted, and with his wife he enjoyed to the full the beauties of his home and superb garden. The sudden death of his wife was a stunning blow to him, for they were great companions. It is some consolation to note that one of his sons is following in his father's footsteps, and is at present in his final year of medicine.

GEOFFREY ASHBURTON THOMPSON.

WE are indebted to DR. GILBERT TROUP for the following account of the career of the late Dr. Geoffrey Ashburton Thompson.

Geoffrey Ashburton Thompson was born in Broken Hill on October 2, 1893. He was the son of Dr. C. Emilius Thompson, an English graduate, who practised in Broken Hill, and who died when his son Geoffrey was only four years old. He was also the nephew of J. Ashburton Thompson, M.D., D.P.H., permanent head of the Department of Public Health in New South Wales for 28 years. It was the courageous effort of his mother and the help of his uncle, financial and otherwise, that permitted his education at Melbourne Church of England Grammar School from 1905 to 1910, and later allowed him to do his medical course at the University of Melbourne, from which he graduated in 1921. After leaving Melbourne Church of England Grammar School in 1910, he carried out clerical work (for the reason set out later by Dr. Farmer) before starting his medical course. His medical student days were interrupted by his enlistment in the forces for the first World War, but the war ended before he could leave Australia and he returned to finish his medical course.

After his graduation in 1921, he came to Perth where he was a resident medical officer at the Perth Hospital (now the Royal Perth Hospital) and subsequently at the Children's Hospital (now the Princess Margaret Hospital). After his hospital work, he was for a short period *locum tenens* for Dr. Yates of Busselton and then for six months for Dr. Dean of Victoria Park. At the end of this Dr. Dean decided to retire, and he sold the practice to Geoffrey Thompson. In this year of 1923, Geoffrey married Constance Josephine Moon. "An ideally mated couple", hackneyed though the phrase may be, is the only way one can describe this happy union. Tragedy struck in the early years of their married life, when their eldest child, Phillip, died from a brain abscess following a middle-ear condition.

In the nine years that followed, the Victoria Park practice was built up at a very rapid rate. In 1926 it had grown to such an extent that Geoffrey took in Tom (now Sir Thomas) Meagher as his assistant and later into partnership. Others that joined the practice over the following years were Bill Peacock, Hildreth Rockett and Hamish McMillan. The last-mentioned finally took over Geoffrey's share of the practice in 1932, when he moved into the full specialization of obstetrics.

It was early apparent in this Victoria Park phase that Geoffrey had an outstanding flair for and leaning towards obstetrics. He quickly realized that the pre-confinement care of the pregnant mother was a major field needing attention, and he focused his original work on this. Obstetrical work flowed to him, and his colleagues soon realized that here was a man who knew more than they did in this branch and were eager to call him into consultation in their difficulties. The stage was reached when he was doing about 400 obstetrical cases per year, and it became impossible, in 1932, for him to carry on any longer in general practice. He thus became the first specialist in obstetrics in Western Australia. Apart from a natural charm of manner, he had the ability to obtain and hold the complete confidence of his patients. Women whom he had

confined years before would relate to me with deep regard and affection their obstetrical history with him. His work indeed typified the finest that could be in a doctor-patient relationship. Geoffrey threw himself into his specialty with a complete disregard of self, and the inevitable happened. In 1937 he became so physically exhausted that he had to make a break. It was difficult to persuade him that this was essential for his future welfare. Reason finally prevailed, and he went overseas for a rest; but even there he could not be prevented from spending several months at the Rotunda Hospital in Dublin.

On his return he was soon as busy as ever. When the second World War got going he could not be kept from enlisting, and in 1941 Perth's foremost obstetrician became Captain Thompson in the 2/12th Australian General Hospital. For 14 months the hospital acted as a staging hospital in Ceylon. The nearest contact to the real war was on Easter Sunday in 1942, when the Japanese dropped some bombs on Colombo, 12 miles away. One can imagine the effect of the sudden transition from the life he had been leading to the dull boredom and often petty irritations of the life of a junior officer in a not very busy staging unit. As a fellow officer I can vouch for the typical Geoffrey Thompson way in which he reacted. He saw humour in most things that occurred and, what is more, got others to see it too. Needless to say, he finished up by being the most popular member of the mess and beloved by men and officers. On the unit's return to Australia in 1943, he was soon and rightly discharged to his more appropriate sphere in civilian life.

For the next eight years he continued, without let up, his over-busy obstetrical life. The details of this and his important work at the King Edward Memorial Hospital are outlined by Dr. Kenneth Worner. How he did it one will never know, but he found time in addition to sit on both the Medical Board and the Nurses' Registration Board of Western Australia for many years. In 1951 it became obvious to those who knew him well that his health had deteriorated to the extent that he could no longer carry on. He developed a cor pulmonale secondary to chronic emphysema and active work became a physical impossibility. His reaction to this was again typical of the man. He adapted himself to the enforced retirement, first by extensive reading on all subjects, a recreation he had never been able by force of circumstances to indulge in adequately. Later he took to clock-mending, and became so highly skilled in this absorbing hobby that he reached the stage when his services were sought after by the professional clock-menders. After exhausting the supply of the decrepit clocks of his numerous friends, he enlisted the aid of the local dustman to keep the supply up. Clocks of all kinds and vintages were scattered round his charming home in Dalkeith.

A year or so after his retirement a coronary occlusion occurred, from which he only slowly recovered. During these years of retirement he was never completely free of, at least, discomfort. It was difficult to keep him within the physical limits that his underlying grave organic condition demanded, and still more difficult to get him to admit to symptoms. He had a horror of causing fuss or bother to anyone, especially anything that would cause worry to his wife Constance. That these years were full of happiness for him was mainly due to her unobtrusive watchfulness and her care and attention of him. He loved his fellow men, and his friends were always dropping in to pass the time of day. It was always a delight to visit him. The end came quite suddenly on the morning of March 2, 1961. He went out like a light, as he would have wished.

Geoffrey Thompson would have been a highly prized asset in any community. To the medically young and isolated Western Australia he was a necessity, and he came at the right time to put modern obstetrics on the map. That he ruined his own health in so doing would cause him no regrets. He placed duty and service to his fellows above all things. His loyalty and charm, his wit, his deep understanding and tolerance of others with less of these virtues made him a friend and companion it is seldom one's good fortune to have in this life. To his wife Constance and his daughter Josephine we offer our deep sympathy in their great loss.

DR. ADRIAN FARMER writes: I would like to add a tribute to my very old friend Geoffrey Ashburton Thompson. We first met at the commencement of our medical course at the University of Melbourne. Geoffrey came of a medical family, but unfortunately lost his father, owing to an accident, when he was only four years of age. His mother, left with two small sons, gallantly decided that they were to have a good education and a university course. Consequently they attended Melbourne Church of England Grammar School from which they matriculated, and whilst Geoffrey's elder brother was completing his engineering course, he obtained employment with an insurance company, as the family purse could not manage both at the university at the one time. Then, in 1914, a happy band consisting of Charles Osborn, Colin Macdonald, Sandy McLorinan, Dick Saltau, Gordon Hislop, Lindsay Male, Bill Frayne and the Madden brothers with us and others, set out on our medical career. The Maddens, later to become well-known grazing and racing identities, owing to their detailed knowledge of the John Wren pony-racing stables, were responsible for our sudden affluence during second year—to such an extent, in fact, that Geoffrey was able to purchase a second-hand motor-cycle, which was a rarity in those days and consequently the cynosure of all.

After qualification and a period of residentship at the Perth Hospital, Geoffrey entered private practice at Victoria Park, where by his skill and devotion to his work he soon converted a large practice into an enormous one, and was one of the first to start a group on a modified basis. It was then that he was drawn to obstetrics, to which he then and later became completely dedicated. "I know this means a full-time job and I shall not be able to enjoy my golf, etc., as you other fellows do", I remember him telling me; and so it was throughout his working life. In those days there was not much medical tuition in Perth, and Geoffrey largely had to learn his obstetrics the hard way by experience in his large practice. Later he attended the Rotunda, and by then he returned as a very competent specialist, building up a reputation which brought him great renown throughout Australia and an honorary Fellowship of the Royal College of Obstetricians and Gynæcologists.

A lonely character was Geoffrey Thompson, so unassuming, so conscientious and such a staunch friend to all that he became the trusted helpmate to all his fellow practitioners and revered by his patients. He lived for and with his work, and his patients all knew it. Naturally in his fifties he was feeling the strain of so much hard work and broken sleep. He told me: "I am going to stop before it is too late, so that my wife and I can enjoy our remaining years." Alas, he was stricken down whilst still in harness, and although he lived on, his activities were very much

curtailed. Nevertheless, he was content, and never so happy as when the younger obstetricians dropped in for a yarn and to glean from his wide experience. He leaves a widow, who equally went with him in his life of social seclusion and to whom he was completely devoted, and a daughter who resides in London. To his great joy, she was visiting her parents during the last two months of Geoffrey's life, and was by her mother's side when the last occlusion came.

DR. KENNETH WORNER writes: I first met Geoffrey Ashburton Thompson in March, 1938, when, as a *locum tenens* in the Fremantle area, I had occasion to seek his advice and help. He seemed genuinely interested in my welfare, and eight years later when I joined him in his specialist obstetric practice, I realized that this interest in people and their welfare came from a deep and abiding love for his fellow man. He was quick to overlook and excuse a fault, equally quick to admire a quality. In his humility he forgot his own many virtues, and strove always to acquire some trait of character or skill which he thought he lacked. He had the happy knack of making every patient feel that she was the only one he had. Likewise, every doctor who called him into consultation was made to feel, not only that Geoff was honoured at being called, but that as well he had learned something from his harassed colleague.

I was closely associated with him in his work for five years, after which ill health forced his retirement. He remained cheerful throughout his long illness, even when confined to bed for almost a year. Geoff Thompson had a sound theoretical knowledge of obstetrics, backed by the widest practical experience of any obstetrician I have ever met, and if one could estimate his worth, I would say that he was in "world class". He was conservative by nature, but knew when to be ruthlessly active if the obstetrical emergency he faced demanded it. He was appointed Honorary Obstetrician at King Edward Memorial Hospital for Women in 1927, and at the time of his retirement in 1951 was Senior Honorary Obstetrician. He loved to talk obstetrics, and long after his retirement his advice was always willingly given whenever colleagues dropped in to discuss their problems. He read assiduously in his retirement and, apart from his general reading, tried hard to bring himself up to date with all branches of medicine.

Geoff was not a regular churchgoer; he had a working knowledge of all the world's religions, and understood and admired all their good points; but his was a truly Christian outlook. He lived close to death for many years, and through it all he retained the virtues of fortitude, cheerfulness, humility and brotherly love. May he rest in peace.

DR. BERTRAM COHEN writes: One of Perth's most popular doctors, Geoffrey Ashburton Thompson, passed away after a long period of ill health on March 2, 1961. He was born in Broken Hill on October 2, 1893. His father, Charles Emilius Thompson, was a specialist surgeon practising in Broken Hill. He died at an early age from an attack of appendicitis, which was not diagnosed. Geoffrey derived his second name from his uncle, Ashburton Thompson, a celebrated Sydney doctor who, amongst other works, carried out researches into bubonic plague in India.

The Thompson family left Broken Hill in 1897 and settled in Melbourne. Geoffrey attended Melbourne Church of England Grammar School as a small boy and remained there until he went to the University of Melbourne. In 1919 he qualified M.B., B.S. His brother Langfear also obtained an engineering degree at the University of Melbourne. He practised as a mining engineer, mainly along the Gold Coast, and subsequently died in London.

After graduating, Geoffrey became a resident medical officer, first at the Perth Public Hospital, and then at the Perth Children's Hospital (now Princess Margaret Hospital for Children). In 1921 he married Miss Constance Moon of Melbourne. After some locum work, he purchased the practice of Dr. Clapperton Dean in Victoria Park. Although for a time he was an honorary out-patient physician at the Perth Public Hospital, from the beginning obstetrics was his main love. He was an acknowledged leader in this specialty, and built up an enormous obstetrical practice. He was an Honorary Obstetrician at the King Edward Memorial Hospital for Women. He carried out post-graduate work at the Rotunda Hospital, and was the first doctor in Western Australia on whom was conferred the Fellowship of the Royal College of Obstetricians and Gynæcologists. His major contribution to obstetrics in Western Australia, apart from his skill in delivery and instruction to students, was the preaching of the doctrine of ante-natal treatment and the establishment of a special department for this aspect of midwifery. He fortunately lived long enough to see the system that he had advocated brought to its present extremely high standard. He had been a member of the Medical Board and of the Nurses' Registration Board. He was a lecturer and examiner in midwifery, and was instrumental in getting St. John of God Hospital registered as a training school.

He retired from practice in about 1950, owing to ill health. During his enforced retirement, his hobby was clock-mending, and there was usually a waiting list of friends and neighbours bringing their timepieces for repair.

His daughter Josephine, B.A. (Melbourne and Oxford), is a competent musician. She completed her nursing training at the Princess Margaret Hospital. At present she is living in England and, in her present occupation, is able to make use of her training in the arts, music and nursing. Ever since his university days, Geoffrey Ashburton Thompson was most popular. He was beloved by patients and colleagues alike. Perhaps the best tribute is contained in the descriptive phrase bestowed on him by Colin Macdonald, which I recall from early days, and with which all who knew him would agree: "The perfect little gentleman."

WILLIAM ADAMSON BOSSENCE.

WE are indebted to DR. L. J. L. PRICE for the following account of the career of the late Dr. W. A. Bossence.

On December 24, 1960, Dr. William Adamson Bossence died while at his work.

"Bill", as he was known to all his friends, was born on April 12, 1905, at Ballarat. He received his education, first at the Brown Hill State School and later at the University High School, where he won the School Exhibition in 1922. From the University High School Bill went to the University of Melbourne, being an "out-patient" at Queen's College. He graduated in 1928. He then became a resident medical officer at the Alfred Hospital for one year, and from there went as a resident to the Fremantle Hospital in Western Australia.

Bill bought a practice in Kyabram in 1933, and remained in this practice until the time of his death. At his work Bill was most efficient, and for many years filled an indispensable place in the district. He was at all times willing to share his great knowledge and skill with the other members of his profession in his district, and I personally shall always remember him gratefully for this.

Bill was a most accomplished musician, and was very much sought after in this capacity. He was always to the forefront in anything musical in the district. He took a great interest in the Kyabram Music Club (which was founded by his wife), and was greatly interested in choir work. He was an accomplished pianist and flautist, but it was in singing that he made his greatest contribution to the entertainment and enjoyment of his fellow men. He had a rich baritone voice and won the *Sun* Aria contest at Geelong in his final year. A brilliant operatic career was forecast for him at this time, but he chose to devote his life to medicine.

On November 14, 1933, he married Mildred Clarke at the Epping Street Peace Memorial Methodist Church, Malvern. There were three children of the marriage, and the only son, Dr. W. H. Bossence, is at present in his father's practice.

During the war Bill spent some time in military service, but did not get overseas.

Probably Bill's greatest interest outside his work and his music was his Lodge. He was Master of the Kyabram Masonic Lodge in 1945-1946. He later received Grand Honours in the United Grand Lodge of Mark Master Masons of Victoria, in which he was Junior Grand Warden. He was also honoured by Grand Honours in the Royal Arch Chapter of Victoria. His sports were golf, fishing and bowls.

He held a prominent place in his church, and was general chairman of a very successful fund-raising campaign for the Kyabram Methodist Circuit in 1956.

It came as a great shock to all his many friends to learn of his sudden and premature end. Much could be said of his magnificent friendliness to all, of his kindness in the troubles of others and of his many outstanding virtues. Their recital would serve to emphasize our loss the more. Perhaps it will suffice to say that we, his friends, mourn his loss very greatly. It will never be quite the same without Bill Bossence.

University Intelligence.

UNIVERSITY OF NEW SOUTH WALES.

Appointments to the Medical School.

THE following further appointments have been made to the Medical School of the University of New South Wales.

Dr. C. P. Wendell-Smith has been appointed Associate Professor of Anatomy. He qualified from St. Bartholomew's Hospital, London, and was awarded the Matthews Duncan Gold Medal on graduation. He has been Assistant Lecturer in Anatomy at the Royal Free Hospital and Lecturer in Anatomy in Guy's Hospital Medical School, from where he has come to the University of New South Wales. His chief research is in neuroanatomy, and he helped to establish the electron microscopy unit at Guy's Hospital. He has published numerous papers and has collaborated in the production of three books.

Dr. C. S. Jones has been appointed Associate Professor of Anæsthetics. He was born in England and qualified at the University of Capetown. He worked at the University of Minnesota and the Mayo Foundation, and later became head of the Department of Anæsthesia in the University of Capetown and its teaching hospitals. Professor Jones is a diplomate of the American Board of Anesthesiology, a Fellow of the American College of Anesthesiology, and a Fellow of the Faculty of Anæsthetists of the Royal College of Surgeons of England. He has written extensively on the subject of anæsthesia, is an indefatigable research worker and is extremely interested in the training of anæsthetists.

Dr. J. B. Johnston has been appointed Associate Professor of (Cardiopulmonary) Surgery. He qualified from the University of Aberdeen, being the most distinguished graduate in 1947. He has had post-graduate surgical experience in hospitals in Aberdeen and Ontario, at Queen's University and at the Mayo Clinic. There he was associated with Dr. Clagett and Dr. Kirklin in their pioneer work on the open-heart closure of atrial septal defects. During three years as Senior Surgical Registrar at the Brompton Hospital and London Chest Hospital, he was allowed to work for a further year at Stanford University as Fellow of the National Institutes of Health (U.S.A.). Professor Johnston has made distinguished contributions in the field of cardiac surgery done under hypothermia and during extracorporeal circulation.

Dr. G. F. Murnaghan has been appointed Associate Professor of (Urological) Surgery. He graduated from the University of Edinburgh after a distinguished course. After several residentships he became Registrar to the Associated Urological Hospitals, London, and was awarded the Vans Dunlop Scholarship for research into the physiology of the ureter. While maintaining continuous contact with clinical surgery, Professor Murnaghan won international recognition for his laboratory research in the field of urology. He was appointed Hunterian Professor of the Royal College of Surgeons of England in 1958. In 1958 he took the degree of Ch.M. (Edinburgh), and in 1961 the degree of M.D. (Edinburgh). He has made numerous contributions to international research journals in the field of urology.

Medical Societies.

MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held on July 14, 1961, at the Medical School of the University of Adelaide, Frome Road, Adelaide.

The Effects of Bradykinin on the Systemic and Coronary Vascular Bed of the Intact Dog.

G. M. MAXWELL, R. B. ELLIOTT and G. M. KNEEBONE discussed the effects of bradykinin on the systemic and coronary vascular bed of the intact dog. It was pointed out that bradykinin, in the circumstances of the study, increased heart rate, cardiac output and coronary blood flow. Systemic, pulmonary and coronary-vascular resistances decreased; those changes were not entirely due to the decrease in systemic and pulmonary arterial pressures. The changes in myocardial oxygen and carbon-dioxide metabolism were mostly related to the increase in coronary blood flow. Bradykinin was found to be associated with a decrease in cardiac efficiency.

The Esterification of ^{14}C-Labelled Cholesterol by R. E. Cells and its Possible Implications in the Pathogenesis of Atheroma.

A. J. D. and P. R. S. GOULD-HURST presented the results of a study in which reticulo-endothelial cells in rat lymph nodes were made to ingest cholesterol-4-^{14}C suspensions. These suspensions were shown to become partially converted by the cells to ^{14}C-labelled cholesterol ester, and in that form to be less readily removed from the cells than free cholesterol. Similar esterification was shown to occur in rabbit reticulo-endothelial cells cultivated *in vitro*. The possible significance of these findings and the inability of reticulo-endothelial cells to oxidize cholesterol were discussed in relation to the pathogenesis of atheroma.

The Mechanism of the Return of Vascular Tone following Sympathectomy in Man.

V. J. PARKS, S. L. SKINNER and R. F. WHELAN discussed a study in which the response of the hand blood vessels had been determined to the intraarterial administration of ephedrine and reserpine, and to the intravenous administration of noradrenaline before and at intervals after sympathectomy. It was pointed out that the constrictor response to ephedrine slowly disappeared over a period of six weeks, during which time the vessels became increasingly sensitive to noradrenaline. The dilator effect of reserpine was abolished early after sympathectomy, but became slowly reestablished over the subsequent three months. The findings suggested that residual vasoconstrictor fibres could not account for the return of tone after sympathectomy, but that changes in the catecholamine content of a peripheral store, and increasing sensitivity to both those and circulating amines, might be closely related to that phenomenon.

Diving Bradycardia in Man.

P. E. HARDING and D. ROMAN discussed a study in which heart rate and blood pressure were measured in adult males during a period of voluntary apnœa lasting for 45 seconds, performed standing both in air and in water at 29° C. It was pointed out that holding the breath in air always caused tachycardia and a fall in blood pressure; holding it while immersed caused bradycardia and a rise in blood pressure. The altered response in water was due to the hydrostatic pressure raising the peripheral resistance. When the breath was then held, blood was trapped in the thorax and the pressure was raised. To compensate, the bradycardia appeared.

Medical Practice.

NATIONAL HEALTH ACT, 1953-1959.

THE following announcements are published in the *Commonwealth of Australia Gazette*, No. 50, of June 15, 1961, and No. 51, of June 22, 1961.

NATIONAL HEALTH ACT 1953-1959.

Notices in Pursuance of Section 134A.

NOTICE is hereby given that, the Medical Services Committee of Inquiry for the State of Queensland, after investigation, having reported on the 10th day of March, 1961, concerning the conduct of Reginald Victor McFadzean, of Clinic Building, Pacific Highway, Burleigh Heads, a medical practitioner, in relation to his provision of medical services under Part IV. of the *National Health Act* 1953-1959, I, Donald Alastair Cameron, Minister of State for Health, did on the third day of May, 1961, reprimand the said Reginald Victor McFadzean.

Notice is hereby given that, the Medical Services Committee of Inquiry for the State of Queensland, after investigation, having reported on the 10th day of March, 1961, concerning the conduct of Patrick Glen McCabe, of Bay-road, Cleveland, a medical practitioner, in relation to his provision of medical services under Part IV. of the *National Health Act* 1953-1959, I, Donald Alastair Cameron, Minister of State for Health, did on the third day of May, 1961, reprimand the said Patrick Glen McCabe.

Dated this third day of May, 1961.

DONALD A. CAMERON,
Minister of State for Health.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JUNE 10, 1961.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	2(1)	2(1)	4(2)	1	..	..	..	..	9
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	1	..	..	..	1	..	2
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	2(2)	1(1)	..	..	..	..	..	..	3
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	5(5)	..	..	3(1)	..	1	..	9
Diphtheria	..	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	..	1(1)	..	..	5(5)	..	..	..	6
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	140(36)	60(36)	16(7)	22(13)	3(2)	4	1	2	248
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	2	..	..	..	..	..	2
Leptospirosis	..	..	..	..	..	..	..	..	..
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	..	..	..	..	..	..	..	..	..
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	..	3(1)	6(4)	..	..	..	..	9
Puerperal Fever	1	..	1	..	..	..	..	..	2
Rubella	..	6(6)	..	..	4(4)	..	..	..	10
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	6(2)	19(9)	2(1)	2(2)	2(2)	..	..	..	31
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	1	..	..	..	1
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	51(38)	9(8)	12(7)	6(4)	1(1)	6(3)	2	..	87
Typhoid Fever	1(1)	..	..	..	..	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JUNE 17, 1961.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	3(2)	..	..	..	1	1	..	5
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	6	..	6
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	11(7)	4(4)	..	3	..	5	..	23
Diphtheria	..	..	..	..	1	..	..	..	1
Dysentery (Bacillary)	..	..	2	4(4)	1(1)	..	..	..	7
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	65(29)	51(23)	12(4)	12(10)	11(6)	5	2	7	165
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	..	..	..	..	..	..	..
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	..	..	..	..	..	..	..	..	..
Ophthalmia	..	..	..	..	..	..	3	..	3
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	2(2)	1(1)	2(2)	..	..	..	..	5
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	15(3)	..	..	2(1)	..	..	..	17
Salmonella Infection	..	..	..	1(1)	1(1)	..	..	..	2
Scarlet Fever	4(1)	10(4)	2	3(3)	..	1	..	..	20
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	1	..	..	..	..	..	..	1
Trachoma	..	..	..	..	104(1)	..	..	..	104
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	18(13)	12(9)	36(20)	2(2)	1(1)	2(1)	1	..	72
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	1(1)	..	..	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Demonstrations in Clinical Neurology.

THE Post-Graduate Committee in Medicine in the University of Sydney, in conjunction with the Medical Faculty of the University of New South Wales, announces that a weekly series of 12 clinical neurological demonstrations will begin on Monday, July 24, 1961, at 4.30 p.m. The demonstrations, which are suitable for candidates preparing for post-graduate qualifications in medicine and in psychiatry, will be conducted by the Department of Neurology and Neurosurgery in the University of New South Wales and held in the Nurses' Lecture Theatre, The Prince Henry Hospital, Little Bay. The fee for attendance is £5 5s. Applications, enclosing remittance, should be sent to the Course Secretary, the Post-Graduate Committee in Medicine, Herford House, 188 Oxford Street, Paddington. Telephone: 31-0671. Telegraphic address: "Postgrad Sydney".

SURGICAL SEMINARS AT ROYAL PRINCE ALFRED HOSPITAL.

SEMINARS are held each Tuesday in the clinical room, Alfred and Mary Roberts Ward, Royal Prince Alfred Hospital, at 4.15 p.m. Professorial Unit rounds commence at 2.30 p.m. and post-graduates are welcome to attend. The programme for July and August, 1961, is as follows: July 18, "Marrow Replacement", Mr. T. S. Reeve, Senior Lecturer in Surgery, Royal North Shore Hospital of Sydney; July 25, "Changing Concepts of Carcinogenesis", Mr. K. W. Starr, M.S., F.R.C.S., F.R.A.C.S., F.A.C.S.; August 1, "Congenital Anomalies of Female Genital Tract", Professor Ulfelder, McIlrath Guest Professor, Royal Prince Alfred Hospital; August 8 and 15, no seminar—Royal Prince Alfred Hospital Reunion; August 22, "Carcinoma of the Anus", Mr. B. P. Morgan, F.R.A.C.S.; August 29, "Management of the Paraplegic Bladder", Mr. H. Learoyd, F.R.C.S.

Notes and News.

Third International Congress of General Practitioners.

The Third International Congress of General Practitioners of the International College of Medical Practice will be held on September 11 to 14, 1961, at Salzburg, Austria. A full and interesting scientific programme has been arranged, and there will be a number of social activities. Further information may be obtained by writing to the Vice-President of the Congress, Dr.med. K. Engelmeier, Langstrasse 21A, Oelde/Westfalen, Germany.

Poliomyelitis Vaccine.

The Minister for Health, Dr. D. A. Cameron, has announced that the Salk vaccine imported from Canada about two months ago has now passed all safety tests prior to being bottled. The vaccine, which was manufactured by the Connaught Laboratories, was imported as a result of difficulties with testing of the vaccine manufactured at the Commonwealth Serum Laboratories. As the Government held that it should not distribute an imported vaccine unless it could itself accept full responsibility for its potency and safety, the Canadian vaccine was subjected to tests at a number of laboratories in Melbourne. Now that these tests have been successful, arrangements are being made for the distribution of the vaccine to State authorities.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Raphael, Margaret Betty, M.B., 1940 (Univ. Sydney), Department of Public Health, 52 Bridge Street, Sydney.

Deaths.

THE following death has been announced:

MASON.—George William Mason, on June 29, 1961, at Surfers Paradise, Queensland.

Diary for the Month.

JULY 17.—Victorian Branch, B.M.A.: Finance Sub-Committee.
JULY 18.—New South Wales Branch, B.M.A.: Medical Politics Committee.
JULY 19.—Victorian Branch, B.M.A.: Clinical Meeting (at Prince Henry's Hospital).
JULY 20.—Victorian Branch, B.M.A.: Executive Meeting of Branch Council.
JULY 20.—New South Wales Branch, B.M.A.: Clinical Meeting.
JULY 21.—New South Wales Branch, B.M.A.: Ethics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): Medical Officers to Sydney City Council. All contract practice appointments in New South Wales. Members are requested to consult the Medical Secretary before undertaking practice in dwellings owned by the Housing Commission.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

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